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A CONVENIENT SYNTHESIS OF FUNCTIONALIZED 1*H*-PYRIMIDINE-2-ONES/THIONES, PYRIDAZINE AND IMIDAZOLE; EXPERIMENTAL DATA AND PM3 CALCULATIONS

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Abstract- The 4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** and semicarbazones and thiosemicarbazones (**2a-h)** combine with loss of carbon dioxide and water yielding the 1-methylenaminopyrimidin-2-one and thione derivatives (**3a-h)** in moderate yields (33-55%). Hyrolysis of **3a** and **3e** leads to the 1-aminopyrimidin-2-one/thione (**4a, b),** pyrimidine (**6**, **11)**, pyridazine (**8**, **13)** and imidazole (**10)** derivatives were obtained from the reactions of **1** and Ethyl-4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate **(12)** with 1,5-diphenylcarbazide **(5)**, 4-phenylsemicarbazide (**7)** and 1-phenylsemicarbazide (**9)**. The electronic and geometric structures of reactants, transition states, intermediates and final products of the reaction of model reactants; 2,3-dihydro-1*H*-furan-2,3-dione and semicarbazone are calculated by the PM3 method. Transition states are further confirmed by vibrational analysis (computation of force constants analytically) and characterised by the corresponding imaginary vibration modes and frequencies.

INTRODUCTION

Concerning the attempts to gain some insight into the chemical behaviour of five membered heterocyclic 2,3-diones against NH-nucleophiles,[1-3] a convenient preparation of functionalized 1*H*-pyrimidine-2-thiones from 4-benzoyl-5-phenyl-2,3-dihydro-2,3-furandione and several thiosemicarbazones has been reported recently.[4] Pyrimidines in general have found much interest for biological and medicinal reasons, thus their chemistry have been investigated extensively.[5] In particularly, various analogues of pyrimidines possess effective antibacterial, antifungal, antiviral, insecticidal and miticidal activities.[6-8] Conformational analysis and quantum chemical

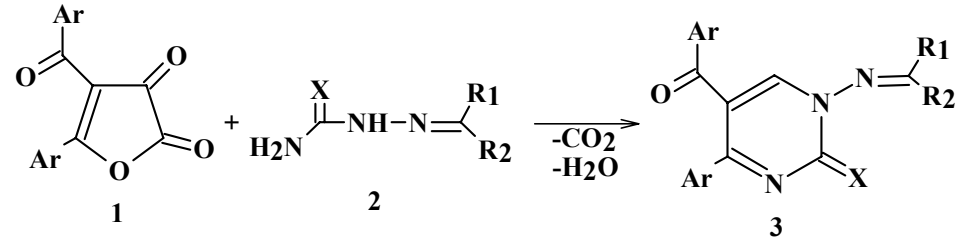
calculations were also carried out by means of semiempirical calculations for the series of compounds being functionalized 1*H*-pyrimidines.[9]

In the present study, we carry out the reactions between semi- and thiosemicarbazones (**2a-h)** and 2,3-dihydro-1*H*-furan-2,3-dione (**1)** and the reaction mechanism for selected model structures have been resulted by semiempirical **PM3** method with full geometry optimisation for reactants, products and intermediates.[10] Transition structures have been located using the linear synchronous transition method contained within SPARTAN program package.[11] Vibrational mode analyses were systematically carried out to confirm that on a potential energy surface all optimized geometries correspond to a local minimum that has no imaginary frequency mode or a saddle point that has only one imaginary frequency mode. Model compounds with aryl and phenyl groups substituted by hydrogen atoms were used in the theoretical calculations. The results of the calculations (the formation entalpies ΔH_f, in kcal.mol^{-1}; dipole moments μ, in debye; the highest and lowest molecular orbital energies E_{HOMO} and E_{LUMO}, in eV and lowest or imaginary frequencies, $\bar{\nu}$ in cm^{-1}) are given in Table 1.

RESULTS AND DISCUSSION

In this paper, the reactions of the 2,3-dihydro-1*H*-furan-2,3-dione (**1)**, easily made from *p,p'*-dimethoxy dibenzoylmethane and oxalyl dichloride,[12] with the semi- and thiosemicarbazones (**2a-h)** are presented and a number of 1,4,5-substituted 1*H*-pyrimidin-2-ones and thiones (**3a-h)** (see Scheme 1) are obtained in moderate yields (33-55 %).

Scheme 1



Ar: *p*-CH3-O-C6H4-

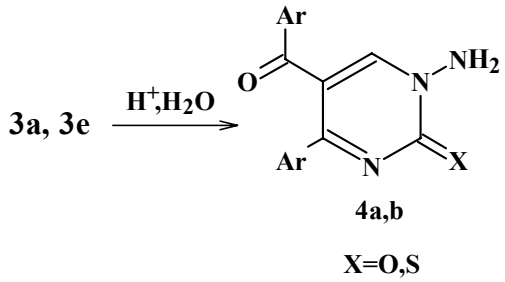
2; 3	X	R1	R2
a	O	-CH3	-Ph
b	O	-H	-Ph
c	O	-CH3	*p*-CH3-O-C6H4-
d	O	-H	*p*-CH3-O-C6H4-
e	S	-CH3	-Ph
f	S	-H	-Ph
g	S	-CH3	*p*-CH3-O-C6H4-
h	S	-H	*p*-CH3-O-C6H4-

The confirmation of the pyrimidine skeleton of **3a-h** is based on an X-Ray study of **3e** [12]. The structural analogy of all compounds (**3a-h)** is easily determined from the elemental analysis, IR, ^{1}H NMR and ^{13}C NMR

spectroscopic data (see Experimental). Product (**3a)** was obtained in 41% yield by treating **1** with acetophenonsemicarbazone (**2a)** and refluxing in boiling toluene for 4 h. The ^{1}H NMR signals were at δ 8.07 (s, 1H, pyrimidine ring). ^{13}C NMR signals were found to be at 192.86 (t, *J=3.9 Hz*, ArCO), 152.29 (s, *J=5 Hz*, pyrimidine C=O) respectively, and elemental analysis data confirms the structure of **3a**.

Hydrolysis of **3a** and **3e** in acetic acid leads to cleavage of the C=N double bond with loss of the corresponding C=O compound finally yielding the aminopyrimidine (**4a,b)** (Scheme 2). In the IR spectra of compound (**4b**), the –NH_2 absorption bands were found to be at about 3250 cm^{-1}. The C=O and C=S absorption bands were at 1660 and 1160 cm^{-1}, respectively. The ^{1}H NMR signals were found to be at δ 10.08, (s, 1H, C6-H), 7.25 (s, 2H, N-NH_2).

Scheme 2

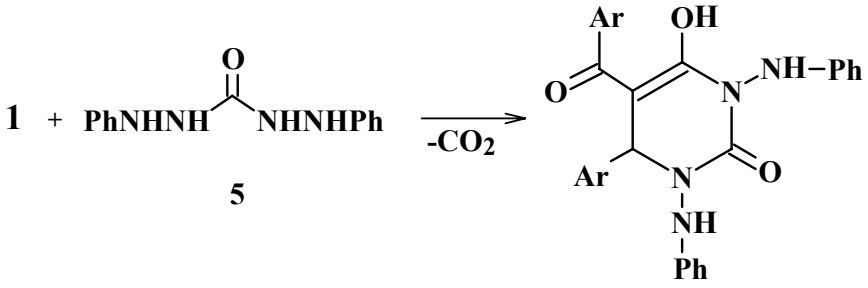


4a,b

X=O,S

In addition to thio- and semicarbazones, in this study, the reaction of 4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** and ethyl4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate (**12)** with 1,5-diphenylcarbazide (**5)** were studied. In the reaction of **1** and **12** with 1,5-diphenyl carbazide (**5**), 1,3-dianiline-4-hydroxy-5-(4-methoxybenzoyl)-6-(4-methoxyphenyl)-1,2,3,4-tetrahydro-2-pyrimidine (**6**) (Scheme 3) and ethyl1-{[4-(ethoxycarbonyl)-5,6-dioxo-2,3-diphenyl-1,2,5,6-tetrahydropyridazine] carbonyl}-5,6-dioxo-2,3-diphenyl-1,2,5,6-tetrahydro-4-pyridazinecarboxylate (**13)** (Scheme 4) were obtained, respectively.

Scheme 3



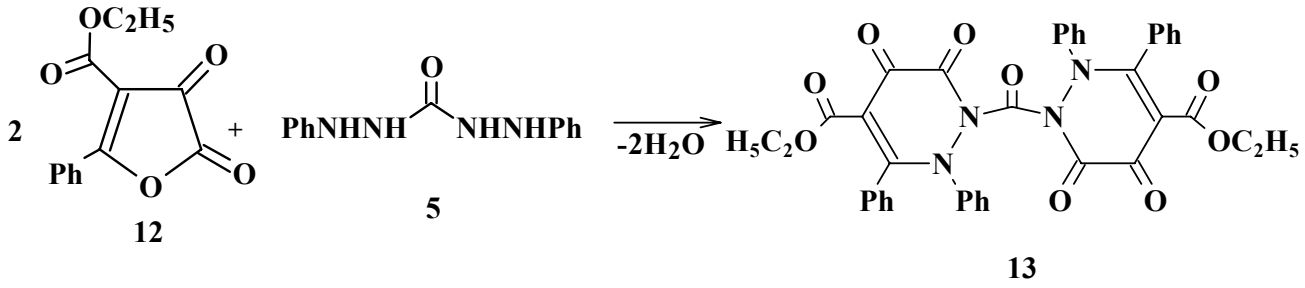
5

6

In the IR spectra of compound (**6)**, -OH and –NH absorption bands were found to be at 3450 and 3300 cm^{-1}, respectively. The ^{1}H NMR signals were found to be at δ 7.92 and 7.88 (s, 2H, -NH) and 5.78 (s, -OH). The ^{13}C NMR signals were at δ 162.15 (s, C-2), 144.47 (s, C-6), and 79.69 (s, C-4). The ^{1}H NMR signals were found to

be at 7.40-7.21 (m, 20H, Ar-H) and 4.22-4.11 (s, -OCH_2). The ^{13}C NMR signals were observed at δ 169.04 (s, C-5), 162.17 (s, C-6) and 64.75 (-OCH_2).

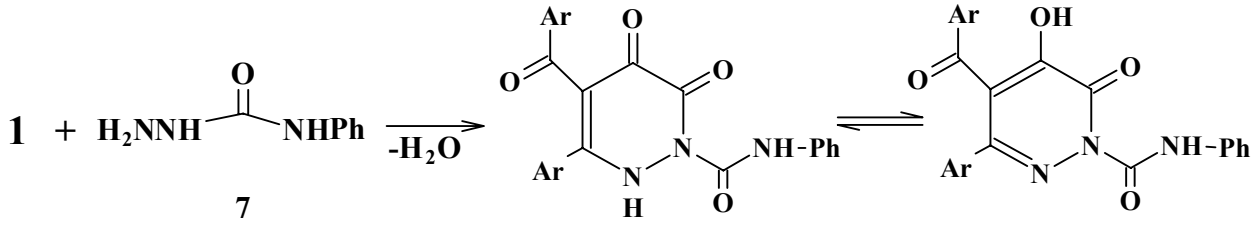
Scheme 4



12 **5** **13**

In another work in this paper, the reaction of **1** and 4-phenylsemicarbazide (**7**) and 1-phenylsemicarbazide (**9**) were studied and as a result of the reaction of **1** and **7** *N*1-phenyl-4-(4-methoxybenzoyl)-3-(4-methoxyphenyl)-5,6-dioxo-1,2,5,6-tetrahydro-1-pyridazinecarboxyamide (**8**) was obtained in 45% yield (Scheme 5).

Scheme 5



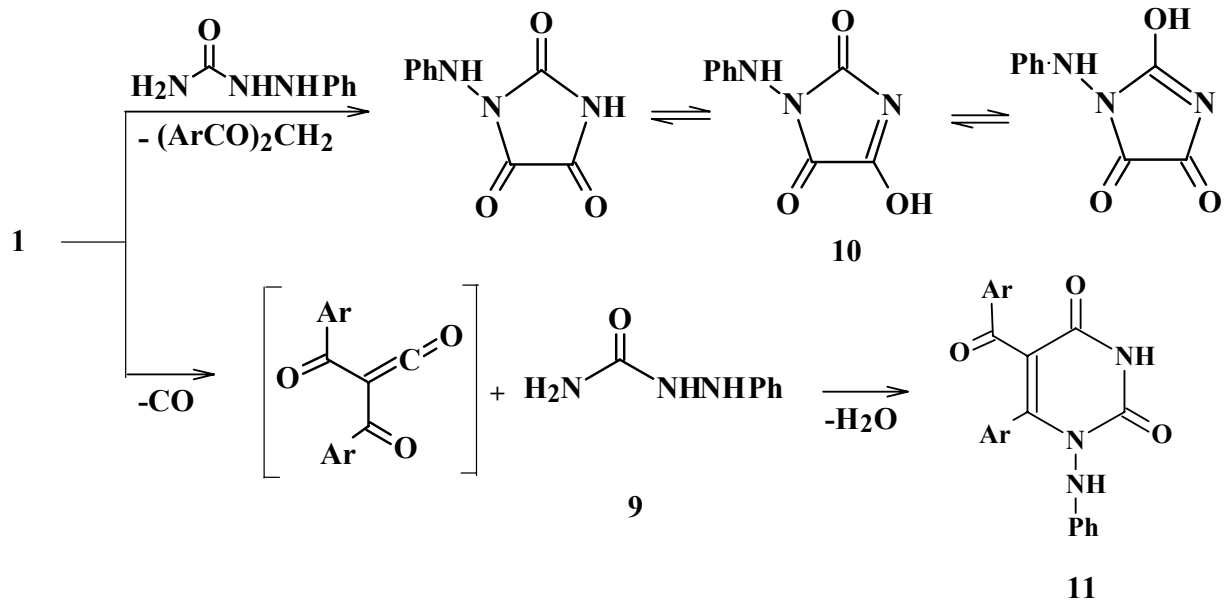
7 **8**

And also the reaction of **1** with **9**, 1-anilinoimidazolidine-2,4,5-trione **(10)** and 1-anilino-5-(4-methoxybenzoyl)-6-(4-methoxyphenyl)-1,2,3,4-tetrahydro-2,4-pyrimidinedione (**11)** were obtained in 48% and 54% yields, respectively (Scheme 6). The thermal decomposition of 4-acyl substituted furan-2,3-diones lead to the α-oxo ketenes as unstable intermediates which undergo addition reaction with nucleophiles.[14] Similarly, the product (**11)** was obtained via the interaction of 1-phenylsemicarbazide with *p,p'*-dimethoxydibenzoylketene intermediate. The spectral data of **8**, **10** and **11** are presented in the experimental part.

A reasonable reaction pathway leading to the pyrimidines (**3a-h**) is briefly outlined in Figure 1. The reaction starts with a nucleophilic attack of the NH_2- group of 2 at the C-5 position of the furandione ring,[1b, 15] similar to a Michael-type addition. Synthesis of pyrimidine systems *via* Michael-type additions of ureas, thioureas, amidines, and similar compounds of this type onto α,β-unsaturated carbonyls are well established.[16] Ring

opening and decarboxylation reaction of an α-oxocarbonic acid intermediate, eventually initiated by the subsequent ring closure *via* addition of the NH to the C=O moiety,[17] and finally loss of water *via* a fragmentational process[18] should be the additional steps.

Scheme 6



The main stages of the presumptive mechanism for the reaction of model structures 4-formyl-2,3-dihydro-1*H*-furan-2,3-dione (**R1**) with semicarbazone (**R2**) and the spatial dispositions of atoms for the reactants, intermediates, transition states and the product calculated by semiempirical PM3 method are shown in Figure 1. According to Figure 1, the interaction of nucleophilic semicarbazone with furandione goes through several stages. Each stage of the reaction is characterized by the electronic properties and energy states (Table 1).

Due to the calculations, it can be suggested that in the reacting system HOMO is represented by the atoms N12, N14 and N15 of the semicarbazone and is located on p_y orbital of N12 with the square of the coefficient 0.07 while the LUMO (-1.68eV) includes the atoms C4, C5 and C3 of the furandione and it is located on the atom C5 with the square of the coefficient 0,36. The LUMO of furan π^*, which is a π antibonding orbital, is strongly polarized to the C5 atom and is relatively low in energy, at least compared with π^* orbital of the semicarbazone, (**R2)**. Thus the larger the square of the coefficient of C5-p_y orbital means that the carbonyl π^* orbital of **R1** will interact strongly with the HOMO of semicarbazone (-9.83eV).

The frontier orbitals localization on the reacting center forces the orbitals energy levels to approach each other. There through, the orbitals interaction increases. It may be suggested that it is precisely the HOMO-LUMO and their constituent atoms C5 and N12 interaction that is the first stage of the reaction (Figure 2).

Figure 1: The Spatial Arrangements of the Atoms for the Reactants, Transition States, Intermediates and Product.

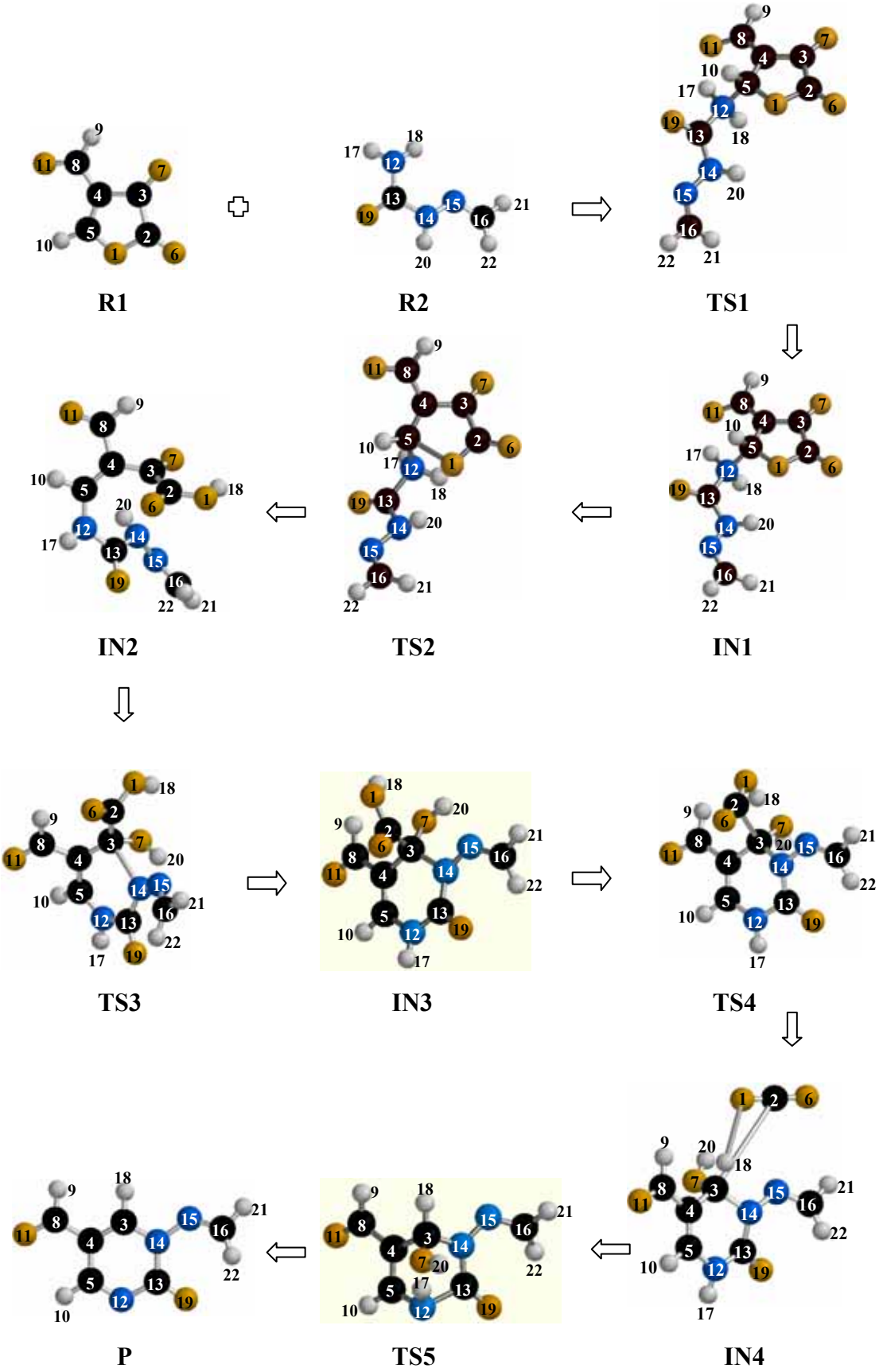
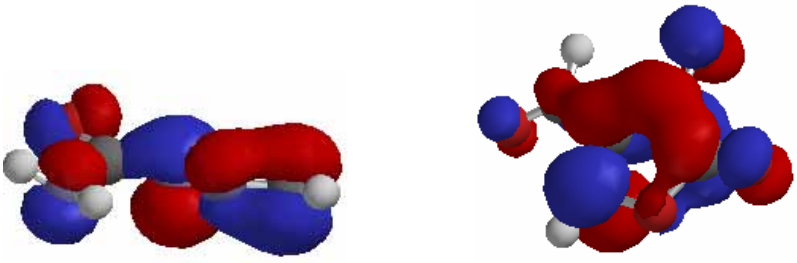


Table 1 Calculated (PM3) Relative Energies, Dipole, HOMO and LUMO Orbital Energies and Imaginary Frequencies for the Reactants, Transition States, Intermediates and Final Product.

Compounds	E_{rel} kcal.mol^{-1}	μ debye	E_{HOMO} eV	E_{LUMO} eV	υ icm^{-1}
R1		1.098	-10.967-	-1.682	
R2		3.117	-9.830	0.350	
R1+R2	0.00				
TS1	23.05	4.529	-9.519	-1.283	**-218.08**
IN1	19.27	5.938	-9.003	-1.349	-
TS2	71.39	8.333	-9.360	-1.743	**-292.25**
IN2	-8.40	1.627	-10.067	-1.235	-
TS3	27.24	5.469	-9.185	-2.201	**-346.74**
IN3	-22.64	2.836	-9.786	-0.872	-
TS4	44.37	2.216	-8.600	-0.931	**-886.79**
IN4+CO_2	-24,41	1.760	-9.557	-0.570	
TS5+CO_2	42,75	5.856	-9.554	-0.694	**-1607.34**
P+CO_2+H_2O	-25,48	4.645	-9.660	-1.220	

Figure 2: Orbitals of R1 (LUMO) and R2 (HOMO)



HOMO of R2 **LUMO of R1**

The reacting molecules, being far from each other (C5-N12: 4Å), thus having no attraction or interaction, have a summary energy (as a system) of -118.16 kcal.mol^{-1} (Table 1) (ΔE_{rel} of **R1**+**R2** is assumed as 0.00 kcal.mol^{-1} for further calculations). When the distance of C5-N12 is equal to 1.90Å, the system passes into the transition state (**TS1)** (ν=218.08 icm^{-1}). Molecular planes of **R1** and **R2** approach at an angle of -59.3°. At that time, the atoms C5 and N12 further approach until the distance 1.605Å transfers the system into a zwitter ion structure, (**IN1)**. The agreement in energy levels between **IN1** (ΔE_{rel}=19.27 kcal.mol^{-1}) and **TS1** (ΔE_{rel}=23.05 kcal.mol^{-1})

leads to the assumption that these molecule structures are similar. **IN1** exists as an unstable reaction intermediate, i.e., a local minimum on the potential energy surface. The 106.6° value of valence angle of C4-C5-N12 at the **IN1** is close to that in sp^3 hybridized carbon and that value is 103.6° for **TS1**. As the interaction of C5-N12 starts, the N12 atom gives the lone pair electrons to the unoccupied orbitals of C5, thus, its charge decreases. The Mulliken charge of N12 is calculated as -0.02ē for compound (**R2)**, 0.14ē for the transition state (**TS1)** and 0.40ē for **IN1** (Table 2). This value at **IN1** proofs the zwitter ion structure, which is a high energy intermediate having no imaginary frequency. The charge on N12 deviates from the expected +1 value because of delocalization of the electrons and the inductive effect. The value of the C5-O1 bond length is 1.42Å and O1-H18 bond length is 2.79Å in **IN1**.

Table 2 Mulliken Charges of the Selected Atoms for the Reactants, Transition States, Intermediates and Final Product

Atomic Charge(ē)	R1+R2	TS1	IN1	TS2	IN2	TS3	IN3	TS4	IN4	TS5	P
O1	-0.21	-0.28	-0.33	-0.63	-0.25	-0.25	-0.25	-0.26	-0.28	-	-
C2	0.22	0.29	0.31	0.41	0.30	0.36	0.31	0.68	0.53	-	-
C3	0.34	0.37	0.40	0.27	0.33	0.37	0.22	-0.34	0.21	0.21	0.03
C4	-0.45	-0.65	-0.75	-0.40	-0.38	-0.42	-0.36	-0.33	-0.35	-0.45	-0.38
O7	-0.23	-0.28	-0.32	-0.24	-0.27	-0.34	-0.30	-0.30	-0.32	-0.22	-
N12	-0.02	0.14	0.40	0.48	0.04	0.28	0.09	0.07	0.08	-0.45	-0.17
C13	0.22	0.19	0.16	0.16	0.20	0.24	0.24	0.20	0.23	0.32	-
N14	0.00	0.02	0.02	0.04	0.001	-0.44	-0.03	0.02	-0.06	-0.15	0.09
H17	0.08	0.11	0.10	0.13	0.11	0.09	0.11	0.10	0.10	0.30	-
H18	0.08	0.65	0.08	0.15	0.22	0.21	0.21	0.40	0.07	0.10	0.14

The transition from **IN1** to **IN2** occurs via the **TS2** structure which is characterized by the presence of a four membered cycle including O1-H18-N12-C5 atoms, produced by the approach of O1 to H18 until the distance 1.85Å leading to the lone pair interaction of the O1 atom to H18 resulting with the bond cleavage of C5-O1. As the O1 interacts with H18 leading to a new bond formation, the O1-C5 bond length increases to 2.14Å and weakens as N12-H18 bond (1.04Å). Imaginary frequency for **TS2** is 292.25 icm^{-1} and ΔE_{rel} is calculated as 71.39 $kcal.mol^{-1}$. Because of the tension of the four centered ring in the transition structure, the activation energy of the system from **IN1** to **IN2** is high and the system readily transfers from the **TS2** structure to the intermediate.

At **TS2** structure, a high negative charge is concentrated on the O1 atom (-0.62ē), while the charge on the atoms O7 (-0.24ē), C3 (0.27ē) and C4 (-0.40ē) decrease because of the electron delocalization. The torsion angle of

C3-C4-C5-N12 is calculated as 130.7° so the system is ready to pass the next stage of the reaction, that is, H18 passes from the atom N12 to the atom O1. The bond cleavage of O1-C5 results an open chain intermediate (**IN2)** (ΔE_{rel}=-8.40 kcal.mol^{-1}). In this structure the value of the bond lengths C4-C5 and O7-C3 decrease after the formation of a new bond O1-H18 (0.95Å). N12-C5-H10 bond angle shows that C5 atom has sp^2 character in this structure. The value of the valence angle of C4-C5-N12 increases (131.6°) after the O2-C5 bond cleavage.

The distance between C3-N14 and O7-H20 atoms are 2.96Å and 3.08Å at **IN2**, respectively. When the C3-N14 bond length becomes 2.11Å, interaction occuring between these atoms leads to the transition state, (**TS3)** (ΔE_{rel}=27.24 kcal.mol^{-1}). The simultaneous attack of N14 to the C3 atom (0.37ē) and shift of the H20 atom from N14 to O7 results with the four centered cyclic ring (ν= 346.74 icm^{-1}) condensed with the six membered pyrimidine ring. The distance between O7 and H20 atoms is calculated as 0.97Å. C3-O7 (1,36Å) and N14-H20 (1,81Å) bond lengths increase at **TS3**. C3 atom is sp^2 characterized in **IN2** structure and the value of the valence angle of C4-C3-O7 at the **IN2** is 123.4°. At **TS3** and **IN3** this value becomes 119.7° and 107.2°. The torsion angle of C3-O7-H20-N14 clearly shows that the atoms are nearly coplanar (20.7°).

The system conversion from **TS3** to the α-oxocarboxylic acid intermediate (**IN3)** (ΔE_{rel}= -22.64 kcal.mol^{-1}) occurs by the bond cleavage of N14-H20 and two new bonds formation C3-N14 (1.41Å) and O7-H20 (0.95Å). The torsion angle of C4-C3-N14-C13 shows this pyrimidine ring being nearly in chair conformation (-31.7°). Concurrent with sp^3 hybridization of C3, the C2-C3-O7 bond angle is calculated as 111.4° and as a result of the single bond arrangement of the C3-O7 bond, the bond length is calculated as 1.40 Å. The bond angle of O1-C2-O6 is calculated as 111.3° for this structure. For the **IN3** structure, the interatomic distance of C2-C3 is 1.57Å and C3-H18 is 2.57°. At that distance there is no interaction between C3 and H18.

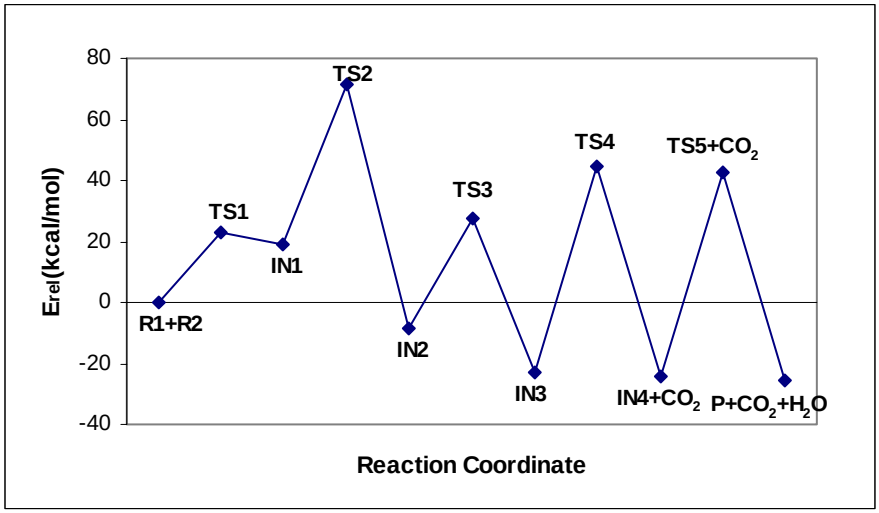
It should be noted that the next step in the reaction process may lead to simultaneous CO_2 and H_2O disconnection. According to the calculations performed to determine the priority of the CO_2 or H_2O separation, the reaction mechanism supporting the separation of CO_2 first and then H_2O is determined to have lower activation energy, thus, is the followed reaction pathway (E_a=67.01 kcal.mol^{-1} for the CO_2 separation first and E_a=73.39 kcal.mol^{-1} for the H_2O separation first). When the C2-C3 cleavage starts, there will be an interaction between C3-H18 atoms leading to a transition state (**TS4)** (υ= 886.79 icm^{-1}, ΔE_{rel}=44.37 kcal.mol^{-1}) at 1.64Å distance. The reacting atoms cause the O1-H18 bond length increase and thus weaken so does the C2-C3 bond (0.95Å, 1.57Å in **IN3** and 1.06Å, 2.38Å in **TS4** respectively). The bond angle of O1-C2-O6 increases during the pathway (111.3°, 163.5°, 179.6° in **IN3**, **TS4** and **IN4**) and O1-C2-C3 bond angle decreases from 122.5° to 79.5° at **IN3** and **TS4,** respectively. The molecular planes of the reacting atoms show that the atoms C2-O1-H18-C3 (torsion angle -0.5Å) are coplanar in **TS4** structure. The atomic charges of the atoms O1 and C2 are -0.25ē and 0.31ē in sequence in the **IN3** structure. O1 atom attracts the bond electrons to itself, thus, the charge on this atom increases at **TS4** (-0.26ē). Consequently, positive charge on C2 increases (0.68ē) at this stage of the mechanism. There exists an intermediate (**IN4)** as a result of the bond cleavage of C2-C3 and O1-H18

(ΔE_{rel}=60.63 kcal.mol^{-1}, **IN4**+CO_2 ΔE_{rel}=-24.41 kcal.mol^{-1}). The changes on the charges of O1 (-0.28ē) and C2 (0.53ē) results from the bond cleavage. Concurrent with the sp^2 hybridization of C2, double bond formation between C2 and O1 takes place (1.18Å) along with the proton transfer from O1 to C3. The bonding state around the C2 shows the linearity of the structure separated.

In the following step, negatively charged O7 (-0.22ē) attacks to the N12-bonded H17 (0.30ē) in order to actualize the H_2O separation, leading to a six membered transition state, (**TS5)** of imaginary frequency υ=1607.34 icm^{-1} (ΔE_{rel}=127,79kcal.mol^{-1}; **TS5**+CO_2 ΔE_{rel}=42.75 kcal.mol^{-1}). The interacting atoms in this structure are located above the pyrimidine system plane as can be seen in Figure 1. The attachment of the O7 to the atom H17 and the N12-H17 bond breaking cause a change in the torsion angle C5-N12-H17-O7 in the system (80.7° at **IN4** and -55.6° at **TS5**). Bond length values 1.54Å for N12-H17 and 1.51Å for C3-O7 are decreased when compared to **IN4** (1.00Å and 1.41Å in sequence) because of the transition to the bond cleavage. The charge on the atom N12 increases during the H_2O separation from 0.08ē **IN4** to -0.45ē **TS5**.

Further separation of the H_2O molecule returns the atom N12 into the state of sp^2 hybridization. The double bond reorganization and proton disconnection from N12 atom occur by this in the system. At this final stage of the reaction mechanism, the pyrimidine skeleton takes a planar configuration due to the π-conjunction in the system (C4-C3-N14-C13: 0.3°) and product (**P)** is obtained (ΔE_{rel}=120,11 kcal.mol^{-1}, **P**+H_2O+CO_2 ΔE_{rel}=-25.48 kcal.mol^{-1}). The bond lengths C3-C4 and C5-N12 are calculated as 1.37Å and 1.31Å which show that of double bonds and the valence angle of C4-C3-N14 is obtained as 120.3° that is close to that of bonds in sp^2 hybridized carbon. In the reaction product (**P)** a decrease in the charges is observed whish is caused by the growth of π-conjunction in the heterocycle.

Figure 3: The Energy Profile of the Reaction Mechanism



In Figure 3 the energy profile of the reaction pathway of the furandion (**R1)** and the semicarbazone (**R2)** molecule is shown. The transition state (**TS2)** possesses the greatest formation energy for the construction of the pyrimidine (**P)** thus, is the rate determining step of this reaction mechanism.

Quantum chemical calculations are used to explain the reaction mechanism and the results enabled us to suggest the reaction of **R1** with **R2** proceeded through some transition states with intermediate formations and a substantial role in the analysis of the paths of the reactions belongs to the interaction of frontier orbitals of reactants. According to the calculations carried out, the theoretical data support the experimental results.

EXPERIMENTAL

Solvents were dried by refluxing with the appropriate drying agent and distilled before use. Melting points were determined on the Electrothermal 9200 apparatus and are uncorrected. Microanalyses were performed on a Carlo Erba elemental analyser, Model 1108; the results agree favourably with the calculated values. The IR spectra were recorded on a Shimadzu Model 435 V-04 spectrophotometer, using potassium bromide discs. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Gemini-Varian 200 instrument. The chemical shifts are reported in from tetramethylsilane and given in δ units.

5-(4-Methoxybenzoyl)-1-(methylphenylmethylenamino)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-one (3a). 4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.4 g, 0.18 mmol) and acetophenonsemicarbazone (**2a)** (0.21 g, 0.18 mmol) were refluxed in toluene (30 mL) for 4 h. The solvent was evaporated and the remaining oily residue was treated with dry Et_2O to give a white crude product which was recrystallized from EtOH and allowed to dry on P_2O_5; yield 0.22 g (41%); mp 178°C; IR (KBr): 3050 (aromatic C-H), 1660 and 1640 (C=O), 800-700 cm^{-1} (pyrimidine ring Skeleton vib.); ^{1}H NMR (DMSO-d_6): δ 8.07 (s, 1H, pyrimidine ring), 7.97-6.72 (m, 13H, ArH), 3.79 and 3.67 (q, 6H, -OCH_3), 2.38 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 192.86 (t, *J*=3.9 Hz, ArCO), 178.25 (s, *J*=3.5 Hz,C-4), 152.29 (s, *J*=5 Hz, pyrimidine C=O), 149.40 (s, C-6), 134.15, (s, C-8), 137.52-115.74 (m, aromatic C), 118.18 (s, C-5), 57.50 and 57.31 (q, $2CH_3O$), 19.61 (CH_3). *Anal.* Calcd for $C_{27}H_{23}N_3O_4$: C, 71.51; H, 5.11; N, 9.27. Found: C, 71.71; H, 5.41; N, 9.04.

5-(4-Methoxybenzoyl)-1-(phenylmethylenamino)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-one (3b). An equimolar mixture of furandione (**1)** (0.6 g, 1.78 mmol) and the corresponding benzaldehydesemicarbazone (**2b)** (0.29 g, 1.78 mmol) were heated at 140^{o}C for 45 min. without any solvent. After cooling to rt, the residue was treated with dry Et_2O and the so formed crude product crystallized from EtOH and allowed to dry on P_2O_5; yield 0.38 g (49%); mp 209°C; IR (KBr): 3000 (aromatic C-H), 1650 and 1640 (C=O), 780-680 cm^{-1} (pyrimidine ring Skeleton vib.); ^{1}H NMR ($CDCl_3$): δ 9.73 (s, 1H, -N=C-H), 8.27 (s, 1H, C6-H), 6.87-6.74 (m,

13H, ArH), 3.82 and 3.76 (q, 6H, -OCH_3); ^{13}C NMR ($CDCl_3$): δ 192.56 (t, ArCO), 171.76 (s, C-4), 154.57 (s, C-2), 151.42 (s, C-6), 134.70, (s, C-8), 134.45-115.78 (m, aromatic C), 118.60 (s, C-5), 57.41 and 57.35 (q, 2CH_3O). Anal. Calcd for $C_{26}H_{21}N_3O_4$: C, 71.04; H, 4.82; N, 9.57. Found: C, 71.04; H, 5.05; N, 9.53.

5-(4-Methoxybenzoyl)-1-(methyl-4-methoxyphenylmethylenamino)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-one (3c).

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.28 g, 0.83 mmol) and *p*-methoxyacetophenonsemicarbazone (**2a)** (0.17 g, 0.83 mmol) were refluxed in toluene (30 mL) for 5 h. The solvent was evaporated and the remaining oily residue was treated with dry Et_2O to give a white crude product which was recrystallized from EtOH and allowed to dry on P_2O_5; yield 0.14 g (35%); mp 206°C; IR (KBr): 3020 (aromatic C-H), 1660 and 1640 (C=O); ^{1}H NMR ($CDCl_3$): δ 8.20 (s, 1H, C6-H), 8.05-6.60 (m, 12H, ArH), 3.85, 3.63 and 3.53 (9H, 3CH_3O-) 2.43 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 191.86 (t, ArCO), 176.25 (s, C-4), 153.29 (s, C-2), 148.60 (s, C-6), 135.15, (s, C-8), 137.72-115.74 (m, aromatic C), 118.38 (s, C-5), 57.55, 57.42 and 57.38 (q, 3CH_3O), 19.71 (CH_3). *Anal*. Calcd for $C_{28}H_{25}N_3O_5$: C, 69.54; H, 5.21; N, 8.70. Found: C, 69.86; H, 5.50; N, 8.76.

5-(4-Methoxybenzoyl)-1-(4-methoxyphenylmethylenamino)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-one (3d).

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.32 g, 0.95 mmole) and *p*-methoxybenzaldehydesemicarbazone (**2d)** (0.18 g, 0.95 mmole) were heated at 140°C for 1 h without any solvent. After cooling to rt, the residue was treated with dry Et_2O and the so formed crude product was crystallized from EtOH and allowed to dry on P_2O_5; yield 0.2 g (45%); mp 217°C; IR (KBr): 3450 (C=O, carbonyl overtone), 3050 (aromatic C-H), 1665 and 1650 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 9.68 (s, 1H, -N=C-H), 8.30 (s, 1H, C6-H), 6.87-6.74 (m, 12H, ArH), 3.82, 3.76 and 3.68 (q, 9H, -OCH_3); ^{13}C NMR ($CDCl_3$): δ 192.44 (t, ArCO), 171.56 (s, C-4), 153.57 (s, C-2), 150.72 (s, C-6), 135.02, (s, C-8), 134.45-115.78 (m, aromatic C), 118.68 (s, C-5), 57.58, 57.46 and 57.40 (q, 3CH_3O). *Anal.* Calcd for $C_{27}H_{23}N_3O_5$: C, 69.06; H, 4.94; N, 8.95. Found: C, 69.20; H, 5.19; N, 8.88.

5-(4-Methoxybenzoyl)-1-(methylphenylmethylenamino)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-thione (3e).

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.32 g, 0.95 mmol) and acetophenonethiosemicarbazone (**2e)** (0.18 g, 0.95 mmol) were heated at 110°C for 60 min. without any solvent. After cooling to rt, the residue was treated with dry Et_2O and the formed crude product was recrystallized from EtOH to give 0.2 g (45%) of a white solid and allowed to dry on P_2O_5; mp 195 °C; IR (KBr): 3020 (aromatic C-H), 1640 (C=O),1150 cm^{-1} (C=S); ^{1}H NMR ($CDCl_3$): δ 7.99 (s, 1H, C6-H), 7.95-6.71 (m, 13H, ArH), 3.79 and 3.74 (q, 6H, -OCH_3), 2.37 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 192.46 (t, *J*=4 Hz, ArCO), 179.87 (s, *J*=3 Hz, C-4), 176.94 (s, C-2), 146.82 (s, C-6), 134.34, (s, C-8), 137.03-115.88 (m, aromatic C), 122.14 (s, C-5), 57.52 and

57.35 (q, $2CH_3O$), 19.63 (CH_3). *Anal.* Calcd for $C_{27}H_{23}N_3O_3S$: C, 69.04; H, 4.94; N, 8.95; S, 8.83. Found: C, 69.34; H, 5.07; N, 8.94; S, 8.56.

5-(4-Methoxybenzoyl)-1-(phenylmethylenamino)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-thione (3f).

An equimolar mixture of furandione (**1)** (0.42 g, 1.24 mmol) and the corresponding benzaldehydethiosemicarbazone (**2f)** (0.22 g, 1.24 mmol) were refluxed in benzene (30 mL) for 135 minutes. After evaporation, the oily residue was treated with dry Et_2O and the formed crude product was recrystallized from EtOH and allowed to dry on P_2O_5; yield 0.31 g (55%); mp 160 ^oC; IR (KBr): 3050 (aromatic C-H), 1640 (C=O), 1170 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 8.97 (s, 1H, -N=C-H), 8.14 (s, 1H, C6-H), 7.91-6.65 (m, 13H, ArH), 3.77 and 3.73 (q, 6H, $-OCH_3$); ^{13}C NMR ($CDCl_3$): δ 192.36 (t, ArCO), 178.37 (s, C-4), 171.97 (s, C-2), 146.98 (s, C-6), 135.63, (s, C-8), 134.18-115.81 (m, aromatic C), 122.07 (s, C-5), 57.36 and 57.53 (q, $2CH_3O$). *Anal.* Calcd for $C_{26}H_{21}N_3O_3S$: C, 69.54; H, 4.65; N, 9.23; S, 7.04. Found: C, 69.84; H, 4.84; N, 8.94; S, 6.84.

5-(4-Methoxybenzoyl)-1-(methyl-4-methoxyphenylmethylenamino)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-thione (3g).

An equimolar mixture of 4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.42 g, 1.24 mmol) and the corresponding *p*-methoxyacetophenonethiosemicarbazone (**2g)** (0.28 g, 1.24 mmol) were refluxed in benzene (30 mL) for 5 h. After evaporation, the oily residue was treated with dry Et_2O to give a yellow crude product which was then recrystallized from EtOH and allowed to dry on P_2O_5; yield 0.21 g (33%); mp 192 ^oC; IR (KBr): 3000 (aromatic C-H), 1660 (C=O), 1160 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 8.15 (s, 1H, C6-H), 8.01-6.60 (m, 12H, ArH), 4.01, 3.70 and 3.65 (9H, $-OCH_3$), 2.30 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 192.52 (t, ArCO), 178.41 (s, C-4), 171.67 (s, C-2), 147.07 (s, C-6), 135.63, (s, C-8), 134.28-115.87 (m, aromatic C), 122.07 (s, C-5), 57.53, 57.43 and 57.36 (q, $3CH_3O$). *Anal.* Calcd for $C_{28}H_{25}N_3O_4S$: C, 67.33; H, 5.01; N, 8.42; S, 6.41. Found: C, 67.12; H, 4.97; N, 8.46; S, 6.11.

5-(4-Methoxybenzoyl)-1-(4-methoxyphenylmethylenamino)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-thione (3h).

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.28 g, 0.83 mmol) and the corresponding *p*-methoxybenzaldehydethiosemicarbazone (**2h)** (0.17 g, 0.83 mmol) were refluxed in benzene (30 mL) for 3 h. After evaporation, the oily residue was treated with dry Et_2O to give a yellow crude product was recrystallized from EtOH and allowed to dry on P_2O_5; yield 0.16 g (40%); mp 179 ^oC; IR (KBr): 3050 (aromatic C-H), 1640 (C=O), 1160 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 8.22 (s, 1H, C6-H), 8.11-6.65 (m, 12H, ArH), 4.01, 3.82 and 3.70 (9H, $-OCH_3$), 2.30 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 192.46 (t, ArCO), 177.87 (s, C-4), 171.77 (s, C-2), 146.68 (s, C-6), 135.83, (s, C-8), 134.28-115.71 (m, aromatic C), 122.07 (s, C-5), 57.53, 57.45 and 57.36 (q, $3CH_3O$). *Anal.* Calcd for $C_{27}H_{23}N_3O_4S$: C, 66.77; H, 4.78; N, 8.66; S, 6.61. Found: C, 66.47; H, 4.77; N, 8.53; S, 6.33.

1-Amino-5-(4-methoxybenzoyl)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-one (4a).

Approximately 15-20 ml of water was added to a solution of **3a** (0.3 g, 0.66 mmol) in 5 mL of AcOH and the mixture was then heated under reflux for 30 minute. With cooling 0.16 g (68%) of **4a** precipitated and was recrystallized from EtOH and allowed to dry on P_2O_5; mp 217 ^oC; IR (KBr): 3250 (-NH_2), 1660, 1640 cm^{-1}(C=O); ^1H NMR ($CDCl_3$): δ 10.02 (s, 1H, C6-H), 8.20-7.43 (m, 8H, ArH), 7.26 (s, 2H, N-NH_2), 3.89 and 3.86 (q, 6H, -OCH_3); ^{13}C NMR ($CDCl_3$): δ 192.28 (t, ArCO), 174.02 (s, C-4), 153.28 (s, C-2), 141.11 (s, C-6), 134.18-115.81 (m, aromatic C), 114.94 (s, C-5), 55.90 and 54.89 (q, $2CH_3O$). *Anal.* Calcd for $C_{19}H_{17}N_3O_4$: C, 64.95; H, 4.84; N, 11.96. Found: C, 65.13; H, 4.80; N, 11.75.

1-Amino-5-(4-methoxybenzoyl)-4-(4-methoxyphenyl)-1*H*-pyrimidin-2-thione (4b).

Approximately 15-20 ml of water was added to a solution of **3e** (0.32 g, 0.68 mmol) in 5 mL of AcOH and the mixture was then heated under reflux for 30 min. With cooling 0.19 g (76%) of **4b** precipitated and was recrystallized from EtOH and allowed to dry on P_2O_5; mp 203 ^oC; IR (KBr): 3250 (-NH_2), 1660 (C=O), 1160 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 10.08 (s, 1H, C6-H), 8.25-7.38 (m, 8H, ArH), 7.25 (s, 2H, N-NH_2), 3.91 and 3.87 (q, 6H, -OCH_3); ^{13}C NMR ($CDCl_3$): δ 192.35 (t, ArCO), 174.22 (s, C-4), 153.28 (s, C-2), 141.11 (s, C-6), 134.18-115.81 (m, aromatic C), 114.74 (s, C-5), 55.91 and 54.89 (q, $2CH_3O$). *Anal.* Calcd for $C_{19}H_{17}N_3O_3S$: C, 62.09; H, 4.66; N, 11.44; S, 8.73. Found: C, 62.20; H, 4.80; N, 11.15; S, 8.45.

1,3-Dianilino-4-hydroxy-5-(4-methoxybenzoyl)-6-(4-methoxyphenyl)-1,2,3,4-tetrahydro-2-pyrimidin (6).

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.34 g, 1.01 mmol) and 1,5-diphenylcarbazide (**5)** (0.17 g, 1.01 mmol) were refluxed in benzene (30 mL) for 2 h. The solvent was evaporated the remaining oily residue was treated with dry Et_2O. The oily residue was dissolved in dry Et_2O. Petroleum ether was then added. The yellow precipitate was filtered off and washed thoroughly with petroleum ether and left to dry on P_2O_5; yield 0.15 g (28%); mp 98 ^oC; IR (KBr): 3450 and 3300 (O-H and N-H), 1660 and 1640 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 7.92 and 7.88 (s, 2H, -NH), 7.70-6.60 (m, 18H, Ar-H), 5.78 (s, -OH) 3.85 and 3.70 (q, 6H, -OCH_3); ^{13}C NMR ($CDCl_3$): δ 193.01 (t, ArCO), 162.15 (s, C-2), 144.47 (s, C-6), 140.87-115.24 (m, aromatic C), 79.69 (s, C-4), 57.44 and 57.18 (q, $2CH_3O$). *Anal.* Calcd for $C_{31}H_{28}N_4O_5$: C, 69.39; H, 5.26; N, 10.44. Found: C, 69.69; H, 5.31; N, 10.73.

***N*1-phenyl-4-(4-methoxybenzoyl)-3-(4-methoxyphenyl)-5,6-dioxo-1,2,5,6-tetrahydro-1-pyridazinecarboxyamide (8).**

4-(4-Methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.43 g, 1.27 mmol) and 4-phenylsemicarbazide (**7)** (0.19 g, 1.27 mmol) were refluxed in benzene (30 mL) for 2 h. The solvent was evaporated and the remaining oily residue was treated with dry Et_2O. The oily residue was dissolved in dry Et_2O. Petroleum ether was then added. The yellow product was then filtered and recrystallized from benzene dried on P_2O_5; yield 0.27 g (45%); mp 119 ^oC; IR (KBr): 3450 and (O-H, enol form) 3250 (N-H, keto form), 1680, 1660, 1650 and 1640 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 10.97-10.86 (s, -OH, enol form), 9.72 (s, -NH, keto form), 7.86 and 6.65 (m, 13H, Ar-H), 3.82 and 3.69 (q, 6H, -OCH_3); ^{13}C NMR ($CDCl_3$): δ 194.63 (t, *J*=4.1

Hz, ArCO), 166.06 (s, keto form, C-5), 162.21 (s, enol form, C-5), 162.13 (s, C-3), 158.75 (s, C-6), 152.38 (s, keto form, C-7), 150.28 (s, enol form, C-7),142.36 (s, C-9), 138.73-113.84 (m, aromatic C), 120.35 (s, C-4), 57.52 and 57.23 (q, $2CH_3O$). *Anal.* Calcd for $C_{26}H_{21}N_3O_6$: C, 66.23; H, 4.49; N, 8.91. Found: C, 66.52; H, 4.56; N, 8.62.

1-Anilinoimidazolidine-2,4,5-trione (10).

When 4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.35 g, 1.04 mmol) and 1-phenylsemicarbazide (**9)** (0.16 g, 1.04 mmol) were mixed and boiled in benzene (30 mL) for 15 minutes. A precipitate was observed. The process was continued up to 40 minutes. The yellow precipitate was filtered and allowed to dry on P_2O_5; yield 0.1 g (48%); mp 238 ^oC; IR (KBr): 3400-3300 (O-H and N-H), 1750, 1730 and 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 8.53 (s, 1H, -OH), 7.38-6.80 (m, 5H, Ar-H), 4.18 (s, 1H, -NH); ^{13}C NMR ($CDCl_3$): δ 159.56 (keto form, C-4), 159.19 (s, C-5), 155.09 (enol form, C-4), 148.07, (s, C-2), 130.64-114.41 (m, aromatic C). *Anal.* Calcd for $C_9H_7N_3O_3$: C, 52.62; H, 3.44; N, 20.48. Found: C, 52.32; H, 3.29; N, 20.19.

1-Aniline-5-(4-methoxybenzoyl)-6-(4methoxyphenyl)-1,2,3,4-tetrahydro-2,4-pyrimidinedione (11).

When 4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-2,3-dihydro-2,3-furandione (**1)** (0.35 g, 1.04 mmole) and 1-phenylsemicarbazide (**9)** (0.15 g, 1.04 mmole) were reacted as the same as **6**. After the separation of the yellow precipitate the residual solvent was evaporated and the remaining oily residue was treated with Et_2O. The yellow precipitate was filtered off and washed thoroughly in dry Et_2O and left to dry on P_2O_5; yield 0.25 g (54%); mp 100 ^oC; IR (KBr): 3350 (N-H), 1660, 1650 and 1640 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 7.72 and 6.34 (m, 13H, Ar-H), 5.83 (s, -NH) 3.78 and 3.69 (q, 6H, $-OCH_3$); ^{13}C NMR ($CDCl_3$): δ 193.10 (t, ArCO), 165.82 (s, C-4), 146.38 (s, C-2), 144.31 (s, C-6), 134.08-115.28 (m, aromatic C), 121.96 (s, C-5), 57.44 and 57.18 (q, $2CH_3O$). *Anal.* Calcd for $C_{25}H_{21}N_3O_5$: C, 67.71; H, 4.77; N, 9.47. Found; C, 67.45; H, 4.57; N, 9.15.

Ethyl1-{[4-(ethoxycarbonyl)-5,6-dioxo-2,3-diphenyl-1,2,5,6-tetrahydro-1-pyridazine] carbonyl}-5,6-dioxo-2,3-diphenyl-1,2,5,6-tetrahydro-4-pyridazinecarboxylate (13).

1,5-diphenylcarbazide (**5)** (0.2 g, 0.82 mmole) was stirred in approximately 35 mL of benzene at rt until it was dissolved. Then ethyl-4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate (**12)** (0.40 g, 1.63 mmole) was added into it. The mixture were stirred for 24 h at 30-35 ^oC. The solvent was evaporated and the remaining oily residue was treated with dry Et_2O. The resulting cream coloured crude product was filtered and recrystallized from CCl_4 and allowed to dry on P_2O_5; yield 0.58 g (51%); mp 170 ^oC; IR (KBr): 1720, 1660 1640 and 1620 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 7.40-7.21 (m, 20H, Ar-H), 4.22 and 4.11 (s, $-OCH_2$), 0.97 and 0.90 (s, 6H, $-CH_3$); ^{13}C NMR ($CDCl_3$): δ 169.04 (s, C-5), 162.17 (s, C-6), 146.33 (s, C-7), 132.21-127.73 (m, aromatic C), 113.79 (s, C-4), 64.75 ($-OCH_2$) and 15.22 (s, $2CH_3$). *Anal.* Calcd for $C_{39}H_{30}N_4O_9$: C, 67.02; H, 4.33; N, 8.02. Found: C, 66.89; H, 4.62; N, 8.32.

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REFERENCES

1. (a) E. Terpetschnig, W. Ott, G. Kollenz, K. Peters, E. M. Peters, and H. G. von Schnering, *Monatsh. Chem.,* 1988, **119**, 367. (b) Y. Akçamur, G. Penn, E. Ziegler, H. Sterk, G. Kollenz, K. Peters, E. M. Peters, and H. G. von Schnering, *Monatsh Chem.*, 1986, **117**, 231. (c) G. Kollenz, E. Ziegler, W. Ott, and H. Igel, *Z. Naturforschg ,* 1976, **31B**, 1511. (d) W. Ott, E. Ziegler, and G. Kollenz, *Synthesis*, 1976, **7**, 477. (e) G. Kollenz, *Liebigs Ann. Chem.*, 1972, **762**, 13.
2. (a) A. N. Maslivets, L. I. Smirnova, and Y. S. Andreichikov, *Zh. Org. Khim.*, 1988, **24**, 1565. (b) V. P. Kruglenko, V. P. Gnidets, N.A. Klynev, and M. V. Povstyano, *Khim. Geterosikl. Soedin.*, 1987, **4**, 533. (c) A. P. Kozlov, V. I. Sychev, and Y. S. Andreichikov, *Zh. Org. Khim.*, 1986, **22**, 1756. (d) Y. S. Andreichikov, D. D. Nekrasov, M. A. Rudenko, and A. Y. Konovalov, *Khim. Geterosikl. Soedin.*, 1987, **6**, 740.
3. İ. Yıldırım and F. Kandemırlı, *Heteroatom Chem.*, 2004, **15**, 9.
4. (a) Y. Akçamur, B. Altural, E. Sarıpınar, G. Kollenz, O. Kappe, K. Peters, E. M. Peters, and H. G. von Schnering, *J. Heterocycl. Chem.*, 1988, **25**, 1419. (b) B. Altural, Y. Akçamur, E. Sarıpınar, İ. Yıldırım, and G. Kollenz, *Monatsh Chem.*, 1989, **120**, 1015. (c) B. Altural and G. Kollenz, *Monatsh Chem.*, 1990, **121**, 677. (d) M. Akkurt, A. Güldeste, H. Soylu, B. Altural, and E. Sarıpınar, *Acta Cryst.*, 1992, **C48**, 315.
5. Recent Rewiews: Brown, D. J. in 'The Chemistry of Heterocyclic Compounds', 'The Pyrimidines', Suppl. II, ed. By A. Weissberger and E. C. Taylor, Interscience Publishers, John Wiley& Sons, 1985, p. 1 ff; D. J. Brown, in: 'Comprehensive Heterocyclic Chemistry', Vol 3, Chapter 2.13, ed. by A. R. Katritzky, C. W. Rees, Pergamon Press, 1984, p.57 ff.
6. C. C. Cheng, *Prog. Med. Chem.*, 1969, 67.
7. D. B. McNair-Scott, T. L. V. Ulbricht, M. L. Rogers, E. Chu, and C. Rose, *Cancer Res.*, 1959, **19**, 15.
8. Sankyo Co., Ltd., Ube Industries, Ltd., Japanese Patent 5936,667[8436,667](*Chem. Abstr.*, 1984, **101**, 1109392).
9. (a) İ. Yıldırım, E. Sarıpınar, Y. Güzel, Ş. Patat, and Y. Akçamur, *J. Mol. Struct., (Theochem)* 1995, **334**, 165. (b) E. Sarıpınar, İ. Yıldırım, Y. Güzel, and Y. Akçamur, *Monatsh Chem.*, 1996, **127**, 505. (c) İ. Yıldırım, M. Tezcan, Y. Güzel, E. Sarıpınar, and Y. Akçamur, *Tr. J. of Chem.*, 1996, **20**, 27.
10. J. J. P. Stewart, *J. Comp. Chem.*, 1989, **10**, 209.
11. PC Spartan Pro., Wavefunction, Inc., Irvine, California, 1999.

12. E. Sarıpınar, Y. Güzel, Z. Önal, İ. Ö. İlhan, and Y. Akçamur, *J. Chem. Soc. Pakistan.*, 2000, **22**, 308.
13. M. Akkurt, E. Sarıpınar, S. Öztürk, Ç. Yılmaz, and H. K Fun, *Z. Kristallogr.*, 2003, **218**, 488.
14. E. Sarıpınar, İ. Ö. İlhan, and Y. Akçamur, *Heterocycles*, 2002, **57**, 1445.
15. Y. Akçamur and G. Kollenz, *Org. Prep. Proced. Int.*, 1987, **19**, 52.
16. A. L. Weis, 'Advances in Heterocyclic Chemistry', Vol 38, ed. by A. R. Katritzky, Academic Press, Inc, 1985, p.45 ff.
17. O. Bayer, 'Methoden der Organische Chemie', Bd. VII/I, Houben-Weyl ed. by D. Müller, Georg Thieme Verlag, 1954, p.317 ff.
18. C. A. Grob, *Angew. Chem., Int. Ed. Engl.*, 1969, **8**, 535.