

## Experimental and theoretical investigations of functionalization and cyclization reactions of 4-benzoyl-5-phenyl-2,3-furandione with some acetanilides

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4-Benzoyl-5-phenyl-2,3-furandione **1** reacts with acetanilides **3a-d** under different conditions and gives the open-chain dibenzoylacetic acid derivatives **5a-c**, **6a,b** and an oxazole derivative **8**. It has been demonstrated that with the variation in reaction conditions the mechanistic course of the reaction changes leading to different products. The electronic structures of the reactants, transition states and final products of the reactions have been investigated on the basis of AM1 and PM3 methods.

Recently, reactions of cyclic oxalyl compounds have been reported to give substituted heterocyclic compounds<sup>1-4</sup>. 4-Benzoyl-5-phenyl-2,3-furandione **1** was obtained by the cyclocondensation of dibenzoylmethane with oxalyl chloride<sup>5,6</sup>. The reactions of substituted 2,3-furandione with various nucleophiles or dienophiles in different solvents and at various temperatures have been studied too<sup>7-10</sup>. Recent years have witnessed the development of a powerful new methodology for the synthesis of substituted aromatic systems and heterocyclic compounds, proceeding through putative ketene intermediates<sup>11-14</sup>. Thermal decomposition of the furandione **1** leads to the formation of reactive dibenzoylketene intermediates<sup>15-20</sup>. A convenient method for the synthesis, and the mechanism of reactions and calculations on the interaction of **1** with several semicarbazones, ureas and their thio-analogs have been reported recently<sup>21-24</sup>.

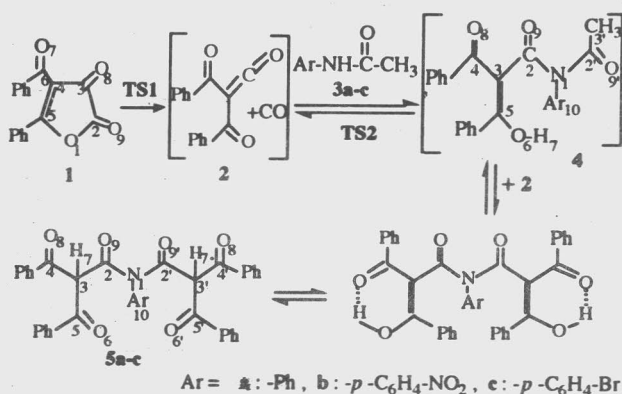
This interest in ketene chemistry is also demonstrated by the recent efforts to extend the MM2 and MM3 force fields to this type of molecules<sup>25</sup>. The general reactivity of ketenes has been reviewed recently, and a few *ab initio* calculations and semiempirical AM1 and PM3 calculations on a series of differently substituted  $\alpha$ -oxoketenes, especially substituent effects on

their stability as well as reactivity, have been published<sup>26-34</sup>.

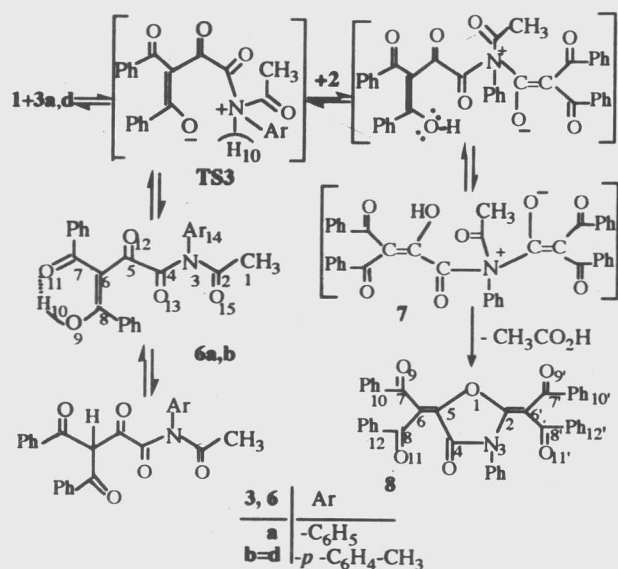
In this paper the reaction of **1** with various acetanilides **3a-d** under different conditions is presented. We have synthesized the substituted amides **5a-c**, **6a,b** and perhydro oxazole derivative **8** (see Schemes I, II) from **3a-d** and **1** and investigated their thermal decomposition and reactivity with anilides at high temperatures.

### Materials and Methods

The reactions were performed in boiling benzene, toluene and xylene either (80-140°C). Obviously, the formation of **5a-c** proceeds through the initial condensation of diacylketene **2**, generated *in situ* from **1** by the thermal elimination



Scheme I



Scheme II

of a CO molecule, with each of the respective acetanilides **3a-c** to the intermediates **4a-c** followed by deacylation and condensation with a second molecule of **2** as depicted in Scheme I. The ketene formation under conditions mentioned has been proved by different workers<sup>15-20</sup>.

The structure of **5** was established by its elemental analysis, and IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectroscopic data (**5a,b** taken as examples). The IR spectra of compounds **5a-c** the C=O exhibited an absorption band at ca. 1700, 1640 cm<sup>-1</sup> (detailed data of **5** are given elsewhere). The IR and NMR spectral data of compounds **5a,b**, indicate the existence of keto-enol tautomerism in these compounds. For example, <sup>1</sup>H NMR spectra exhibited signals the range δ 8.3-7.9 ppm and 3.34 ppm, and <sup>13</sup>C spectra showed peaks at δ 148.18, 147.41 and 110.83, 104.34 ppm (C-3, C-3'). These weak peaks indicate in favour of keto-enolic forms of the compounds **5a,b**.

Changing the conditions of the reaction results in different final products. Unlike the reaction, under which the ketene is formed in the first stage, the attack on the substrate **1** by the nucleophiles **3a, d** proceeds without preliminary elimination of CO.

Besides the thermolysis reactions, the compound **1** also reacted with numerous NH-nucleophiles<sup>4,10,21</sup>. The substituted amide derivative **6a,b** were obtained in 25% and 40% yields,

respectively from the nucleophilic addition reactions of **1** with acetanilide **3a** and *p*-methylacetanilide **3d** under heating in benzene for 4 hr (see Scheme II).

In addition, the product **8** was formed from **1** and **3a** as the reaction period increased. As shown in Scheme II, the diacylketene **2** is added to TS3 and a stable oxazole ring is formed by the elimination of a molecule of acetic acid. The elemental analyses and spectroscopic data of **8** agreed well with the proposed structure.

**Method of Calculation.** To study the mechanism of the reaction, all calculations were carried out by means of semiempirical AM1 and PM3 methods with full geometry optimization for reactants and products. The criterion for terminating all optimizations was increased 100-fold over normal MOPAC limits using the PRECISE option. A configuration interaction (CI) within an AM1 formalism was carried out using a CI=4 configuration. These CI calculations were performed by keeping the same geometries as obtained at the Hartree-Fock level.

Transition states were approximately located by the reaction-coordinate method. The cycloreversion rather than the cycloaddition reaction was used, keeping the length of one of the breaking bonds constant while varying the other one; all other parameters were optimized, and stationary points were refined by the norm of energy minimization. So, in each stationary point the system was characterized by the corresponding Hessian (force constant) matrix, calculated and diagonalized. The standard parameters<sup>35-37</sup> and the programs<sup>38</sup> were used in the AM1 calculations. The AM1 and PM3 calculations were carried out with the help of MOPAC program package<sup>38</sup>. Model compounds with phenyl groups substituted by the hydrogen atoms were used in the theoretical calculations.

**Reagents and Instrumentation.** Melting points were determined on an Electrothermal 9200 apparatus and are uncorrected. Elemental analyses were performed on a Carlo-Erba 1108 of Hewlett Packard, CHNS model 105 analyser. IR spectra were obtained in potassium bromide pellets on a Shimadzu Model 435 V-04 spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Varian XL 200 Gemini spectrophotometer using

tetramethylsilane (TMS) as internal standard (chemical shifts in  $\delta$ , ppm). All experiments were followed by TLC using Alufolien Kieselgel 60 F G F<sub>254</sub> (Merck) and spots visualised under Model Camag TLC lamp (254/366nm). Solvents were dried by refluxing with appropriate drying agents and distilled before use. Solvent and other chemical reagents were obtained from Merck, Sigma, Aldrich and Fluka. 4-Benzoyl-5-phenyl-2,3-furandione **1** was prepared according to the literature procedure<sup>5</sup>.

**Synthesis and Experimental Data: *N,N*-Bis (dibenzoyl acetic acid)-*N*-phenyl amide **5a**.** A mixture of 4-benzoyl-5-phenyl-2,3-furandione **1** (0.5 g, 1.8 mmoles) and acetanilide **3a** (0.243 g, 1.8 mmoles) was refluxed in boiling xylene for 1 hr. From the liquid phase the precipitated light yellow crystals were filtered and recrystallized from acetic acid to give 0.426 g (40%) of **5a**, m.p. 238° [Found: C, 77.13; H, 4.42; N, 2.20. C<sub>38</sub>H<sub>27</sub>NO<sub>6</sub> (593.64) requires C, 76.90; H, 4.55; N, 2.36 %]; IR (KBr): 3600-3200 (hydrogen bonded O-H), 3050s (C-H aromatic superimposed by O-H stretch), 1700 s, 1640 s (C=O, amide and ketonic), 1590 m, 1470 s' (C=C) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO);  $\delta$  8.00-7.90 (q, 2H), 7.69-7.04 (m, 25H, aromatic), 3.34 (s, 2H, under the peak of H<sub>2</sub>O in DMSO probably); <sup>13</sup>C NMR (DMSO);  $\delta$  195.30 (s, C-4), 194.34 (s, C-4'), 175.89 (s, C-2), 174.94 (s, C-2'), 160.82 (s, C-5), 157.53 (s, C-5'), 148.18 (s, C-3, C-3', in enol-form), 138.51, 137.92, 137.41, 136.21, 135.35 (m, *N*-Ph), 133.51-129.11 (m, C-Ph's), 110.83 (s, C-3, C-3', in keto-form).

***N,N*-bis (dibenzoyl acetic acid)-*N-p*-nitrophenyl amide **5b**.** A solution of **1** (0.5 g) and *p*-nitroacetanilide **3b** (0.26 g) (molar ratio 1:1) in toluene was refluxed for 4 hr. Evaporation of the solvent provided an oily residue which was triturated with anhydrous Et<sub>2</sub>O to give a crude white solid. It was recrystallized from acetic acid yielding **5b** 0.459 g (40%), m.p. 328°C [Found: C, 71.63; H, 4.02; N, 4.10. C<sub>38</sub>H<sub>26</sub>N<sub>2</sub>O<sub>8</sub> (638.64) requires C, 71.47; H, 4.07; N, 4.39 %]; IR: 1680 s, 1640 s (C=O), 1590 m, 1530 m, 1450 s (C=C) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO);  $\delta$  8.30-8.25 (d, 2H), 8.04-7.05 (m, 24H, aromatic), 3.34 (s, 2H, belong to O-H under the peak of H<sub>2</sub>O in DMSO, probably); <sup>13</sup>C NMR (DMSO);  $\delta$  205.29 (s, C-2, C-2'), 194.07 (s, C-4, C-4'), 160.68 (s, C-5, C-5'), 147.41 (s, C-3,

C-3', in enol-form), 142.85-123.48 (m. aromatic C), 104.34 (s, C-3, C-3', in keto-form).

***N,N*-Bis (dibenzoyl acetic acid)-*N-p*-bromophenyl amide **5c**.** A solution of **1** (0.5 g) and *p*-bromoacetanilide **3c** (0.35 g) (molar ratio 1:1) in benzene was refluxed for 4 hr. After evaporation, the oily residue was treated with dry Et<sub>2</sub>O. The precipitated crude red product was filtered and recrystallized from acetic acid to give **5c** 0.423 g (35%), m.p. 274° [Found: C, 68.23; H, 3.52; N, 2.05. C<sub>38</sub>H<sub>26</sub>NO<sub>6</sub>Br (672.54) requires C, 67.85; H, 3.86; N, 2.08%]; IR (KBr): 3050 w (C-H aromatic), 1700 s, 1660 m (C=O), 1600 m, 1540 s, 1460 m (C=C), 1320 s (C-O).

**3,3-Dibenzoyl-2-oxopropanoic acid-*N*-acetyl-*N*-phenyl amide **6a**.** Reaction of **1** (0.5 g, 1.8 mmoles) and **3a** (0.243 g, 1.8 mmoles) was carried out by refluxing in boiling benzene for 4 hr and evaporation of the solvent left the oily residue which was treated with dry Et<sub>2</sub>O. The resultant precipitate was filtered and recrystallized from methanol yielding **6a** 0.185 g (25%), m.p. 155° [Found: C, 72.81; H, 4.82; N, 3.54. C<sub>25</sub>H<sub>19</sub>NO<sub>5</sub> (413.43) requires C, 72.63; H, 4.63; N, 3.39 %]; IR (KBr); 3050 w and 2950 w (C-H, aromatic and aliphatic), 1710 s, 1670 s (C=O), 1580 m, 1480 m, 1450 m (C=C) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>);  $\delta$  7.94 (d, 1H), 7.90-7.27 (m, 15H, aromat), 2.05 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>);  $\delta$  193.78 (d, C-7, C-8), 175.32 (d, C-4, C-5), 170.66 (s, C-2), 140.52 (s, C-6, in enol-form), 138.10, 135.61 (q, *N*-Ph), 131.97-129.16 (m, C-Ph, aromatic C), 67.92 (s, C-6, in keto-form), 28.27 (s, C-1).

**3,3-Dibenzoyl-2-oxopropanoic acid-*N*-acetyl-*N-p*-methylphenyl amide **6b**.** Reaction of **1** (0.5 g, 1.8 mmoles) and *p*-methyl acetanilide **3d** (0.243 g, 1.8 mmoles) was carried out in boiling benzene for 4 hr. Removal the solvent gave an oily residue which was treated with dry Et<sub>2</sub>O and the precipitate filtered and recrystallized from methanol, yielding **6b** 0.295 g (40%), m.p. 181° [Found: C, 72.99; H, 5.15; N, 3.42. C<sub>26</sub>H<sub>21</sub>NO<sub>5</sub> (427.46) requires C, 73.06; H, 4.95; N, 3.27]; IR (KBr): 3050 w and 2950 w (C-H, aromatic and aliphatic), 1710 s, 1670 s (C=O), 1580 m, 1480 m, 1450 m (C=C) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO):  $\delta$  8.22-8.19 (d, 1H), 8.05-7.19 (m, 14H aromat), 2.32 (s, 3H), 2.15 (s, 3H); <sup>13</sup>C NMR (DMSO):  $\delta$  193.72 (d, C-7, C-8), 174.48 (d, C-4, C-5), 170.21 (s, C-2),

140.27 (s, C-6, in enol-form), 137.62, 137.45, 135.46 (q, N-Ph), 131.96-130.16 (m, C-Ph, aromatic C), 67.18 (s, C-6, in keto-form), 27.83 (s, C-1), 22.44 (s, C-15).

**2,5-Bis (dibenzoyl methylene)-3-phenylperhydro-oxazol-4-one 8.** Under the same procedure as described for **5c** (only the reaction period was 7-8 hr), the reaction of **1** and **3a** (molar ratio 1:1) 0.379g (35%) gave **8** which was crystallized from acetic acid, m.p. 230° [Found: C, 77.96; H, 4.14; N, 2.22. C<sub>39</sub>H<sub>25</sub>NO<sub>6</sub> (603.64) requires C, 77.66; H, 4.16; N, 2.32 %]; IR (KBr): 3050 w (C-H aromatic), 1710 s, 1640 m (C=O), 1600-1450 (C=C), 1340 s, 1100 m (C-N, C-O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 7.98-6.64 (m, aromatic H's) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 194.61 (s, C-7, C-8), 177.92 (s, C-4), 164.26 (s, C-2), 162.88 (s, C-5), 138.66, 138.05, 136.65, 135.95, 135.68 (m, C-6, N-Ph, exchangeable), 133.64-128.10 (C-Ph's, aromatic C).

## Results and Discussion

As may be inferred from calculations, the opening of furandione **1** cycle with simultaneous CO elimination occurs at the first stage of the reaction resulting in ketene **2** formation. Selected electronic and structural data for the systems investigated are given in Tables I-IV. Additional

computations were carried out taking into account the configuration interaction. According to the data obtained, the values of  $\Delta H_f$  and  $\mu$  did not undergo substantial changes. The virtual orbitals inclusion changes the energy of MO levels. A common depression of MO levels is observed for all systems, but the order of levels is the same.

As seen from Tables I and II, the elimination of CO molecule is realized through a transition state (**TS1**) with the value of  $\Delta H_f$  equal to -71.14 kcal/mol. The search for the transition state in MOPAC was performed with the SADDLE option and then the structure obtained was subjected to optimization by NLLSQ, followed by thermodynamic and vibrational analysis.

The **TS1** is formed when the atom C2 moves to the distances of 1.95Å and 1.89Å from the atoms C3 and O1, respectively. The energy of activation barrier is found to be 27.74 kcal/mol (see Figure 1).

The difference in the energies of the initial compound and the sum of the two final products is equal to 20.49 kcal/mol (see Figure 2). The full elimination of the molecule CO is observed under distances C2 - C3 = 3.89Å and O1-C2 = 3.50Å.

Two alternative mechanisms of **2+3** interaction were considered. One of them is the two-step mechanism. In the first stage the nucleophile is

Table 1—Enthalpies of formation ( $\Delta H_f$ ), dipole moments ( $\mu$ ) and ionization potentials (IP) calculated for the reactant **1**, intermediates and the products

	SCF			SCF + CI		
	$\Delta H_f$ (kcal/mol)	$\mu$ (Debye)	IP (eV)	$\Delta H_f$ (kcal/mol)	$\mu$ (Debye)	IP (eV)
<b>1</b>	-99.31	1.27	11.12	-99.40	0.64	15.09
<b>TS1</b>	-71.57	1.39	10.40	-81.77	2.65	14.01
<b>2+CO</b>	-78.80	3.12	10.51	-73.51	1.49	14.03
<b>2+3</b>	-126.43	4.85	10.33	-126.40	4.85	15.51
<b>CTS2</b>	-112.52	6.09	9.30	-113.17	6.26	13.64
<b>4</b>	-135.18	4.70	10.76	-124.46	4.49	13.82
<b>1+3</b>	-143.41	7.60	10.90	-145.62	7.44	14.45
<b>CTS3</b>	-120.51	5.03	10.42	-115.44	8.48	13.58
<b>6</b>	-161.90	4.57	10.28	-165.01	5.52	13.71
<b>7</b>	-207.85	8.08	9.30	-208.18	8.05	13.14
<b>TS4</b>	-148.89	9.48	9.02	-148.92	9.46	12.69
<b>I4</b>	-187.87	10.96	8.65	-187.89	11.04	12.20
<b>TS5</b>	-172.23	9.45	8.81	-172.24	9.44	12.37
<b>8</b>	-239.01	2.85	10.11	-241.04	2.78	13.62

Table II— Structural parameters of the reactant 1, transition states and final products, corresponding to Scheme I.

	1	TS1	2		2+3	TS2	4
Bond length							
O1-C5	1.383	1.263	1.235	O6-H7	2.611	1.849	0.971
O1-C2	1.427	1.892	3.500	O6-C5	1.233	1.251	1.351
C2-C3	1.529	1.952	3.890	N1-H7	0.987	1.036	2.656
C3-C4	1.477	1.371	1.339	N1-C2	4.038	1.577	1.398
C4-C5	1.371	1.453	1.460	N1-C2'	1.372	1.483	1.403
C4-C6	1.454	1.460	1.465	C2-C6	1.343	1.414	1.486
C6-O7	1.233	1.234	1.232	C2-O9	1.175	1.227	1.242
C3-O8	1.220	1.176	1.177	C2'-C3'	1.508	1.496	1.501
C2-O9	1.212	1.176	1.169	C3-C5	1.460	1.432	1.353
				C3-C4	1.460	1.459	1.471
Bond angles							
C2-O1-C5	107.77	105.20	121.64	O6-H7-N1	103.16	138.47	122.62
O1-C2-C3	107.42	92.69	64.62	H7-N1-C2	102.04	107.14	69.93
C2-C3-C4	105.31	100.59	102.01	N1-C2-C3	105.60	115.78	119.65
C4-C3-O8	125.58	153.77	179.84	C3-C2-O9	179.26	135.53	121.90
C3-C4-C6	120.11	119.53	120.19	H7-N1-H10	117.94	109.26	112.62
				H7-N1-C2	121.84	106.68	103.71
				C2-C3-C4	121.76	118.93	117.23
Torsion angles							
C5-O1-C2-C3	-0.14	0.63	2.09	C2-N1-H7-O6	3.84	29.41	66.24
C5-C4-C3-O8	0.23	0.15	0.06	C2-C3-C4-O8	0.67	8.15	24.59
				H7-N1-C2'-O9'	176.64	-137.21	-109.52

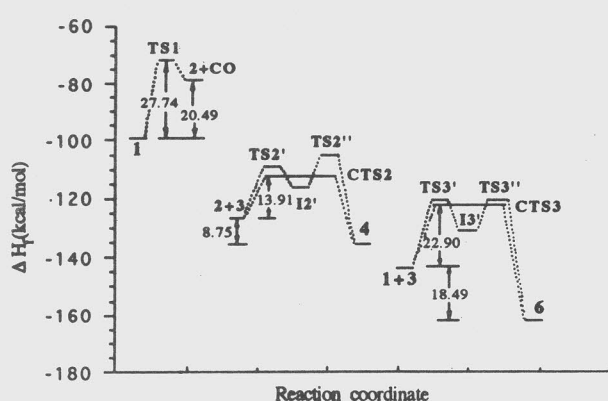
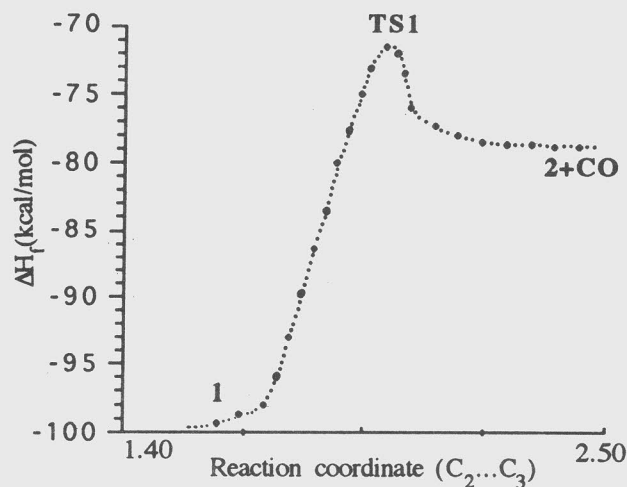


Figure 1—Activation barrier values for the main stages of the reactions (see Schemes I and II).

added to the atom C2, and then a proton H7 passes to O6. In this way two transition states  $TS2'$ ,  $TS2''$  and an intermediate state  $12'$  are formed.

The second alternative is realized through a concerted mechanism with simultaneous bond  $N1...C2$  and  $O6...H7$  (concerted transition state

Figure 2—Potential energy profile for the reaction  $1 \rightarrow 2+CO$ .

$CTS2$ ) formation. According to AM1 and in view of transition state theory, the concerted mechanism is favoured by 2 kcal/mol over the two-step mechanism. The spatial arrangements of the atoms in the transition and intermediate states are shown

in Figure 3.

The  $\Delta H_f$  dependence on the reaction coordinates for both mechanisms is presented in Figure 4a,b.

Transition to the molecule **2** causes the bond angle C4-C3-O8 to increase (for compound **2** it is equal to  $179.84^\circ$ ) and the atom C3 is converted from  $sp^2$ -state to the linear  $sp$  hybrid state. The molecule **2** obtained is planar, and the torsional angle C5-C4-C3-O8 is equal to  $0.06^\circ$ .

In the second stage a nucleophile is combined with **2** resulting in the transition state CTS2. With this the atom N1 of the nucleophile attacks the atom C2 with the formation of new bonds and breaking of the old ones. As seen from the data in Table II, the formation of the bonds N1-C2 and O6...H7 leads simultaneously to the weakening of the bond N1-H7. The transition state CTS2 ( $\Delta H_f$  - 112.52 kcal/mol) is characterized by the presence of a six-membered cycle with the bond lengths substantially changed as compared with their initial values.

For CTS2 the distances N1-C2, N1-H7 and O6-H7 are  $1.58\text{\AA}$ ,  $1.04\text{\AA}$  and  $1.85\text{\AA}$ , respectively. Further approach of the atoms N1 and C2 leads finally to the formation of the bonds N1-C2 and O6-H7 and the breaking of the bond N1-H7. The activation barrier for this reaction is found to be 13.91 kcal/mol, and the difference in the energies of the initial compound and the sum of two final products is equal to 8.75 kcal/mol (see Figure 1).

As Table II shows, the reaction results in the rearrangement of bonds and valence angles in the reacting systems. The values of valence angles of carbon and nitrogen atoms are close to the values of angles for  $sp^2$  hybrid bonds. The torsional angle C2-N1-H7-O6 equal to  $66.24^\circ$  clearly shows that the atoms are not coplanar.

The structure elucidation of **6a** is mainly based on H-coupled  $^{13}\text{C}$  NMR spectroscopy: signals at  $\delta$  193.78 (d, C-7, C-8), 175.32 (d, C-4, C-5), 170.66 (s, C-2), 140.52 (s, C-6, in enol-form), 67.92 (s, C-6, in keto-form), and 28.27 (s, C-1) could be assigned to the main chain-carbons of **6a**. For details of spectroscopic investigations see experimental data.

In the same way, two alternative mechanisms for **1+3** interaction are also considered (see Figure 5a,b).

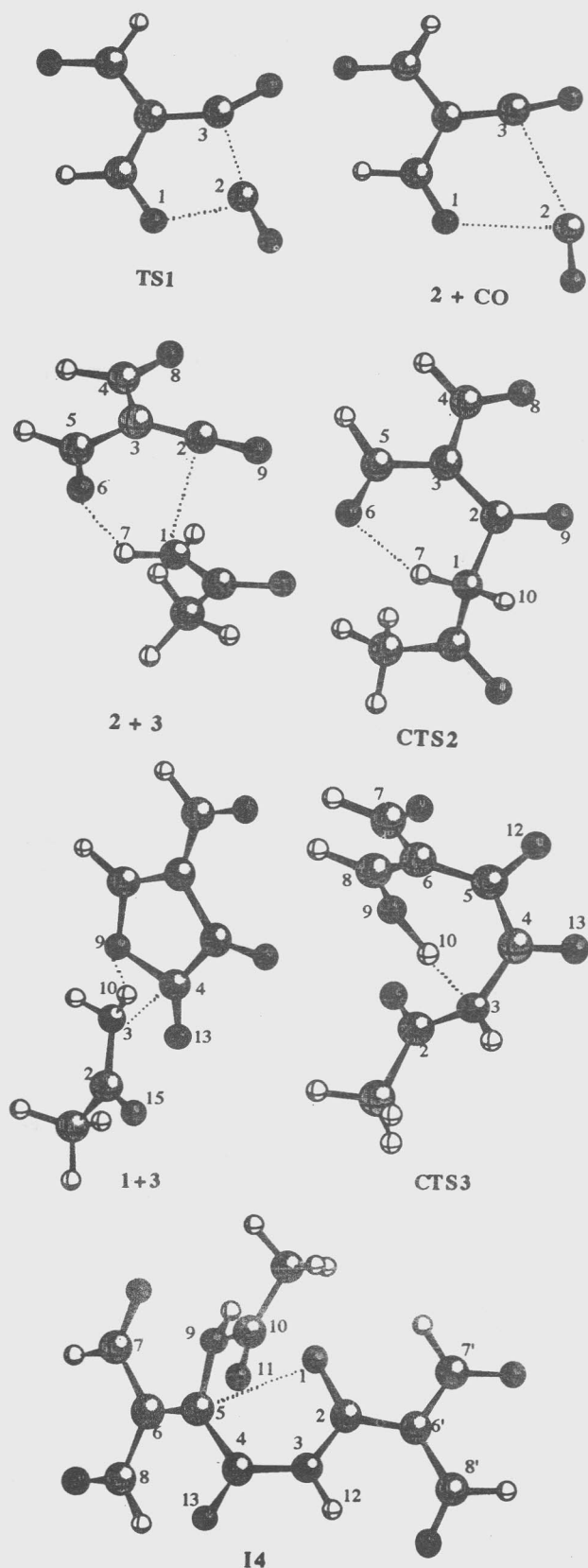


Figure 3—Spatial disposition of atoms for the transition and intermediate states.

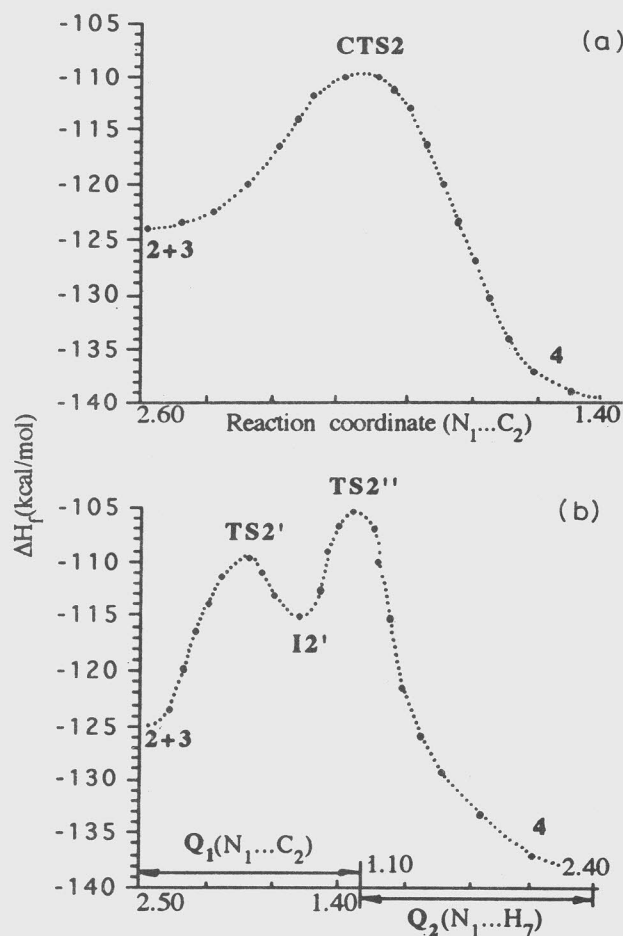


Figure 4—Potential energy profile for the reaction 2+3 [(a) Concerting mechanism; (b) two-step mechanism].

The first one is the synchronous concerted path when both processes mentioned occur simultaneously. The alternative path is the step-by-step reaction. When simulating the processes of synchronous binding with the formation of **6** through two-step mechanism, we found out that the concerted mechanism was more preferable. The formation of two transition states **TS3'** and **TS3''** and one intermediate state **13'** is characteristic of the two-step mechanism. The concerted mechanism goes through the **CTS3** formation.

The variations of structural characteristics for the reacting molecules are given in Table III. The transition state **CTS3** involves the formation of a seven-membered ring. In this state, the distances **N3-C4** and **N3-H10** are 1.45 Å and 1.55 Å, respectively. The valent angle **N3-H10-O9** comes

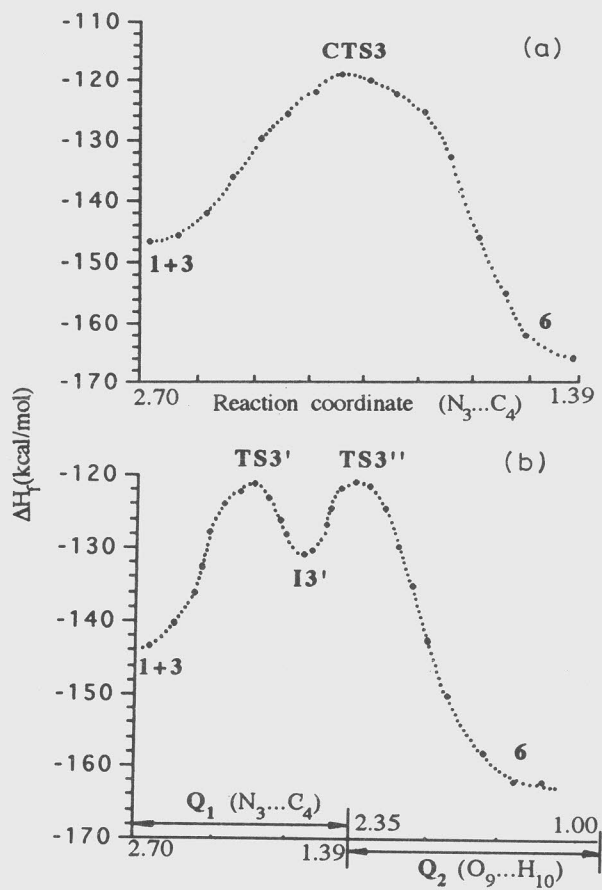


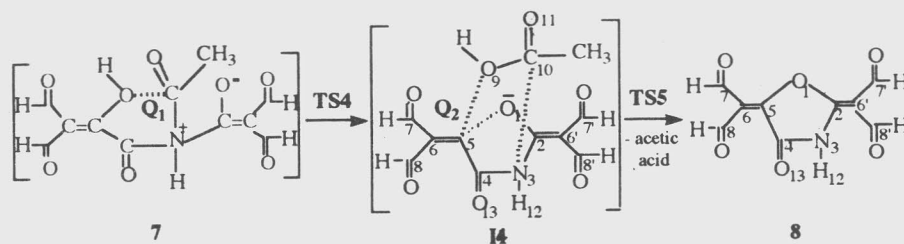
Figure 5—Potential energy profile for the reaction 1+3 [(a) Concerting mechanism; (b) two-step mechanism].

to 147.96°, and the angle **C6-C8-O9** becomes 128.59°.

The resting angles in the transitional seven-membered ring are close to 120°. The activation barrier is 22.90 kcal/mol. From a comparison of the energies of reactants and the product **6**, it follows that the reaction is exothermic ( $\Delta H_f = 18.49$  kcal/mol). The atom **N3** approaching to the atom **C4** causes the jump of the proton **H10** from **N3** to **O9**. In the final product the lengths of the bonds **N3-C4** and **O9-H10** are 1.39 Å and 0.98 Å, respectively. Due to this the valent angle **C8-O9-H10** is reduced to 112.05° and the torsional angle **N3-H10-O9-C8** is increased to -33.69°.

The  $\Delta H_f$  dependence on the reaction coordinates for both mechanisms is shown in Figure 5a, b.

A study of the transition from **7** to **8** (see Scheme III) has shown that the process goes, step by step, through a number of transition and intermediate states. Preliminary calculations have



Scheme III.

shown that in the first stage the carbon atom C10 more likely is attacked by the oxygen atom O9 belonging to the hydroxyl group.

The  $\Delta H_f$  variations depending on the bond O9...C10 length are shown in Figure 6, and the structural parameters of the intermediates are given in Table III. As seen from Figure 6, the system goes through the transition state **TS4** and forms the intermediate state **I4**.

In the intermediate state the atom O9 approaches C10 at the distance 1.401Å. Due to

this, the length of the bond N3-C10 increases, and the bond C5-O9 becomes loose. Simultaneously, the atoms O1 and C5 approach each other. In the second stage of the reaction the growth of the bond C5-O9 length leads to the elimination of CH<sub>3</sub>COOH molecule and ring closure through the atoms O1 and C5, producing the stable product **8**. Thus, the system goes through the transition state **TS5** ( $\Delta H_f = -172.23$  kcal/mol).

Experimental investigations of the NMR spectra of compounds **5** have shown the presence of keto-

Table III— Structural parameters of the reactants, transition states and final products corresponding to Schemes II and III

Bond length	1+3a	TS3	6a		7	TS4	I4	TS5	8
C2-N3	1.397	1.443	1.406	O1-C2	1.235	1.251	1.280	1.284	1.415
N3-C4	2.730	1.451	1.386	O1-C5	4.518	3.105	2.543	2.310	1.412
N3-H10	0.992	1.547	3.965	C2-N3	1.578	1.518	1.425	1.426	1.388
C4-C5	1.532	1.451	1.529	N3-C4	1.482	1.460	1.371	1.368	1.412
C4-O9	1.431	2.555	3.265	N3-C10	1.503	1.727	3.138	3.272	3.805
C4-O13	1.212	1.229	1.248	C4-C5	1.508	1.502	1.510	1.493	1.511
C5-C6	1.483	1.446	1.466	C4-O13	1.226	1.224	1.244	1.246	1.228
C6-C7	1.454	1.469	1.477	C5-O9	1.350	1.433	1.447	1.756	3.15
C8-O9	1.385	1.334	1.347	C5-C6	1.361	1.343	1.350	1.329	1.345
O9-H10	2.350	1.144	0.975	O9-C10	2.682	1.402	1.401	1.392	1.369
				C10-O11	1.225	1.256	1.214	1.218	1.231
Bond angles									
C2-N3-H14	115.10	116.43	117.54	O1-C2-N3	112.01	112.13	115.40	113.71	109.50
N3-H10-O9	124.29	147.96	122.20	C2-N3-H12	107.40	112.24	116.61	119.72	122.76
N3-C4-O13	85.86	120.98	118.62	N3-C10-O9	72.82	100.71	74.60	77.92	59.61
C5-C6-C8	108.41	121.25	125.83	N3-C10-O11	116.08	107.26	73.52	67.58	59.99
C6-C8-O9	113.40	128.59	128.53	C4-C5-O9	110.96	105.70	117.67	114.02	98.20
C8-O9-H10	104.90	122.17	112.05	C5-O9-C10	91.22	117.00	121.62	121.23	141.73
Torsion angles									
C5-C6-C8-O9	0.62	11.67	1.50	O1-C2-N3-H12	-156.30	172.64	-173.57	-174.26	-176.31
C8-O9-H10-N3	-99.29	-15.18	-33.69	N3-C10-O9-C5	-49.04	2.52	32.97	18.67	15.42
C6-C8-O9-H10	80.94	14.46	-5.31	C6-C5-O9-C10	-156.15	-170.51	161.76	175.80	-145.73
O9-H10-N3-H14	109.36	74.54	-123.91	O9-C5-C4-O13	-177.71	158.39	125.46	115.51	107.08



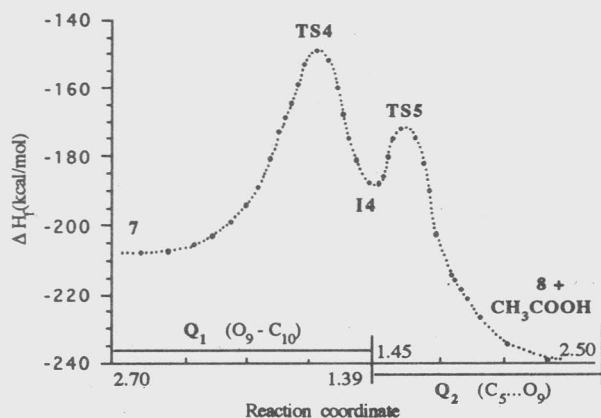
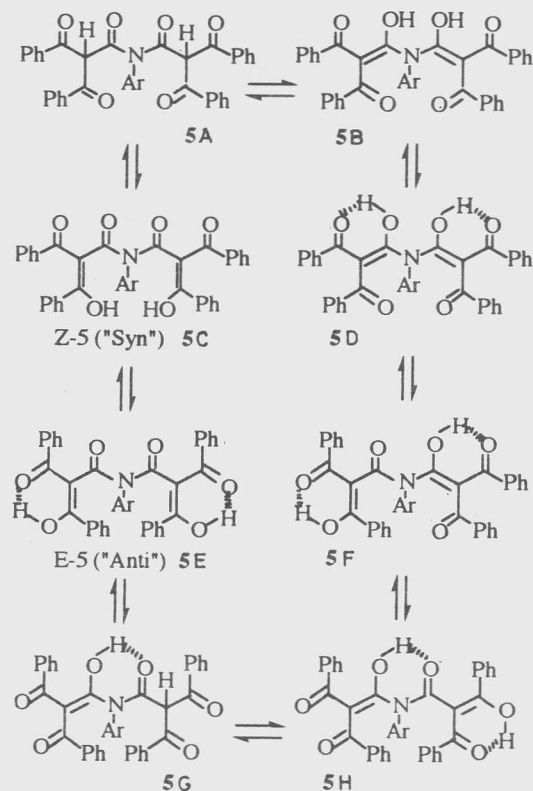


Figure 6—Potential energy profile for the transition from 7 to 8.

enol tautomerism. To make it clear if different keto-enol forms are stable, we give here the results of the electronic structure calculations done by the methods AM1 and PM3 for different model compounds (see Scheme IV).

According to the data calculated (see Table IV), stability of the systems mentioned depends upon their ability to form intramolecular hydrogen bonds. As seen from Table IV, formation of two hydrogen bonds stabilizes the molecule.

The value of  $\Delta H_f$  almost remains unchanged when the system passes from keto-form **5A** to enol-form. Substantial changes are observed for the dipole moments of **5A** and **5C**. A comparison of the isomers *Z* (**5C**) and *E* (**5E**) shows that *E*-form with high value of  $\mu$  is more stable than *Z*-form ( $\Delta\Delta H_f = 9$  kcal/mol).



Scheme IV

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Table IV—Enthalpies of formation ( $\Delta H_f$ ), dipole moments ( $\mu$ ) and ionization potentials (IP) calculated for the keto-enol tautomers **5A-H**

Tautomer	AM1			PM3		
	$\Delta H_f$ (kcal/mol)	$\mu$ (Debye)	IP (eV)	$\Delta H_f$ (kcal/mol)	$\mu$ (Debye)	IP (eV)
<b>5A</b>	-192.13	1.77	11.21	-205.71	1.19	10.92
<b>5B</b>	-190.48	1.17	9.77	-205.00	2.52	9.43
<b>5C(Z-)</b>	-189.07	8.53	10.48	-198.46	6.96	10.17
<b>5D</b>	-196.24	0.15	9.80	-212.37	0.61	9.47
<b>5E(E-)</b>	-198.80	4.56	10.73	-211.02	3.77	10.50
<b>5F</b>	-200.59	2.41	9.93	-215.81	2.49	9.64
<b>5G</b>	-193.21	4.78	10.03	-207.68	4.21	9.85
<b>5H</b>	-200.87	4.83	9.81	-213.51	4.26	9.63

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