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INVESTIGATION OF THE MECHANISM OF THE HETEROCYCLIZATION OF 1-HETEROBUTADIENYLKETENES USING THE MINDO/3, MPDP, AND AM1 METHODS

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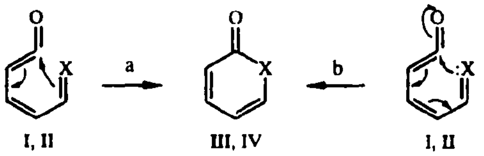
The semiempirical MINDO-3, MPDP, and AM-1 methods are shown to be applicable to the calculation of the cyclization of 1-oxa- and 1-azabutadienylketenes. The mechanisms of the heterocyclizations have been studied. Formation of the new σ*-bond results from interaction of the unshared electron pair of the heteroatom with the* π^*_x *of the ketene* $C=O$ *bond.*

The heteroanalogs of 1,3,5-hexatrienes, in which the terminal double bond is in the ketene group, are highly reactive compounds which cyclize to heterocycles even as they are formed [1]. They are intermediates in the rearrangements of six-membered heterocycles [1, 2]. Cyclization of these compounds is part of the strategy for original syntheses of pyrimidinones, oxazines and quinolones [2]. A study of the rules for the cyclization of 1-heterobutadienylketenes disclosed the possibilities inherent in a greater understanding of the rearrangements of six-membered heterocycles for the synthesis of new pyranones and pyridones and their heteroanalogs, some of which possess considerable biological activity [3].

There are a number of unresolved problems in the chemistry of these compounds. For example, it is unclear why substitution of a heteroatom in the terminal methylene group of butadienylketenes accelerates cyclization. It is also unclear by which mechanism formation of the new σ-bond is formed: (a) by electrocyclic or (b) by interaction of the unshared pair of the heteroatom X and the empty π^*_x orbital localized on the carbon of the ketene group, analogously to the cyclization of imidoylketene [4].



To shed light on these problems we have carried out quantum chemical calculations on the cyclizations of 1-oxa- (I) and 1-aza-1,3,5-hexatrien-6-ones (II) into 2-pyranes (III) and 2-pyridones (IV) respectively. The energy barriers and the structures of the transition states of these reactions were determined using the method of reaction coordinates [5]. Calculations were carried out using the semiempirical MINDO-3 [6], MPDP [7] and AM1 [8] methods. Geometric characteristics of the compounds were obtained by complete optimization of the geometry by the Bryden–Fletcher–Goldfarb–Shanno method [9].

CYCLIZATION OF 1-OXO-1,35-HEXATRIENE(I) AND 2-PYRANE(III)

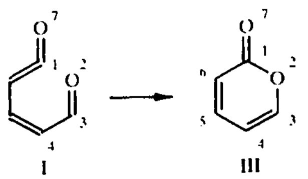


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TABLE 1. Geometric Parameters for the Reaction I → III Obtained by the MPDP Method

Parameter	Structure									
	1	2	3	4	5	6	7	8	9	10
Bond Length, Å										
$C_{(1)}-O_{(2)}$	2,885	2,850	2,647	2,484	2,181	1,970	1,748	1,624	1,452	1,390
$O_{(2)}-C_{(3)}$	1,228	1,227	1,230	1,223	1,237	1,250	1,274	1,278	1,291	1,353
$C_{(3)}-C_{(4)}$	1,475	1,474	1,484	1,471	1,462	1,448	1,435	1,430	1,415	1,370
$C_{(4)}-C_{(5)}$	1,361	1,358	1,363	1,366	1,372	1,377	1,430	1,347	1,341	1,450
$C_{(5)}-C_{(6)}$	1,443	1,442	1,434	1,449	1,437	1,421	1,399	1,395	1,382	1,363
$C_{(6)}-C_{(1)}$	1,340	1,340	1,337	1,350	1,359	1,370	1,440	1,435	1,446	1,400
$C_{(1)}-O_{(7)}$	1,175	1,175	1,173	1,174	1,177	1,181	1,188	1,189	1,202	1,224
Bond Angle, deg										
$O_{(2)}-C_{(3)}-C_{(4)}$	126,61	125,90	120,88	121,30	121,88	122,00	121,35	121,34	120,74	122,20
$C_{(3)}-C_{(4)}-C_{(5)}$	131,84	130,70	124,97	122,91	122,09	121,40	120,76	120,55	119,82	119,70
$C_{(4)}-C_{(5)}-C_{(6)}$	131,96	133,10	134,88	131,63	126,74	125,10	124,40	123,95	123,03	118,80
$C_{(5)}-C_{(6)}-C_{(1)}$	130,22	129,50	131,81	133,03	131,02	126,90	120,41	120,04	117,37	120,30
$C_{(6)}-C_{(1)}-C_{(7)}$	175,06	175,40	174,60	173,31	166,49	158,10	153,75	143,35	135,88	113,90
E_{act}	-28,1141	-28,1586	-25,7167	-23,579	-19,9867	-17,6326	-19,1331	-29,0259	-39,3919	-39,3919

TABLE 2. Changes in the Atomic Charges Along the Reaction Coordinate I → III, Calculated by the MPDP Method

Structure	Atomic Charge						
	$C_{(1)}$	$O_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$O_{(7)}$
1	0,37	-0,34	0,31	-0,25	0,13	-0,31	-0,11
2	0,37	-0,34	0,31	-0,25	0,12	-0,30	-0,11
3	0,38	-0,36	0,31	-0,26	0,13	-0,31	-0,12
4	0,40	-0,37	0,31	-0,27	0,13	-0,32	-0,12
5	0,43	-0,39	0,32	-0,29	0,15	-0,34	-0,13
6	0,46	-0,39	0,33	-0,33	0,17	-0,36	-0,16
7	0,46	-0,37	0,29	-0,36	0,17	-0,31	-0,20
8	0,44	-0,31	0,28	-0,33	0,14	-0,30	-0,24
9	0,39	-0,24	0,22	-0,27	0,09	-0,23	-0,29
10	0,37	-0,24	0,15	-0,21	0,04	-0,17	-0,31

The distance between atoms $C_{(1)}$ and $O_{(2)}$ was chosen as the reaction coordinate because the $C_{(1)}-O_{(2)}$ bond is the only one formed during the cyclization. The bond lengths, bond and interplane angles for the initial and final structures were calculated in the normal way. All geometric parameters were then optimized for 10 intermediate structures along the reaction coordinate. Calculations of the Gauss matrix for the initial, final and transition (TS) states confirmed that the initial and final states corresponded to minima on the potential energy surface (PES) and that the transition state corresponded to one of the negative terms in the Gauss matrix [10]. The activation enthalpies calculated by the MINDO-3, MPDP, and AM1 methods were 7.85, 10.32, and 2.66 kcal/mol. Comparison with the experimental activation energy (9.4 kcal/mol) [11] showed that the MINDO/3 and MPDP methods gave satisfactory agreement with the experimental value for the activation energy, whereas the AM1 method did not.

The results of the MPDP calculations for the bond lengths and bond angles for the heavy atoms are given in Table 1. In Tables 1-4, structure 1 corresponds to the reactant, structure 5 to the intermediate, and structure 10 to the reaction product. The calculated interplane angles are not given in the tables because all the heavy atoms and the hydrogen atoms on $C_{(3)}$ and $C_{(6)}$ are in one plane. According to the criteria given in [12, 13], the position of these hydrogen atoms in the transition state in the plane of the molecule or out of that plane indicates whether the cyclization is disrotatory or conrotatory. The calculations show that the cyclization does not occur by rotation of the terminal atoms relative to the terminal π-bonds of the triene systems.

Charges, π-atomic occupancy and squares of the appropriate vectors of the boundary orbitals were calculated for the ten structures lying on the reaction path by the method of steepest slope from the transition state to the initial and final structures (Tables 2 and 3). The calculations show that the π structure of the molecule changes little on approaching the transition state and rearrangement of the π system occurs only after the $C_{(1)}$—$O_{(2)}$ bond has reached a length of 1.97 Å. Bonds $O_{(2)}$—$C_{(3)}$, $C_{(1)}$—$C_{(6)}$, $C_{(4)}$—$C_{(5)}$ increase in length and bonds $C_{(3)}$—$C_{(4)}$ and $C_{(5)}$—$C_{(6)}$ decrease in length. From an analysis of the changes in π atomic occupancy and atomic charges it appears that different processes occur before and after reaching the transition state: before the value of the coordinate reaches 1.9 the atomic charge decreases on atoms $C_{(1)}$, $C_{(3)}$ and $C_{(5)}$ and increases on atoms $O_{(2)}$, $C_{(4)}$ and $C_{(6)}$. Then, after the transition state has been achieved, the reverse process is observed: charges increase on $C_{(1)}$, $C_{(3)}$ and $C_{(5)}$ and decrease on atoms $C_{(2)}$, $C_{(4)}$ and $C_{(6)}$. Evidently, in the first stage of the cyclization (from 2.85 to 1.9) an alternating change in charges in the conjugated π-system occurs as is usually observed when a π donor substituent is introduced into an aromatic system, while in the second stage, (from 1.9-1.4) when the new σ-bond is formed, the π system is reconstructed. It is formed from the unshared pair of electrons on the oxygen atom, perpendicular to the plane of the molecule, and the formation of new double bonds, $C_{(3)}$—$C_{(4)}$ and $C_{(5)}$—$C_{(6)}$.

Values for the squares of the vectors corresponding to the nonbonding orbitals of $O_{(2)}$ and π^* $C=O$ of the ketene group, at right angles to the orthogonal π system of the molecule are given in Table 4. It can be seen that, after the reaction coordinate has reached a value of 1.9 Å, there is a rapid decrease in the occupancy of these orbitals which confirms the conclusion these orbitals participate in the cyclization process and in the formation of the $C_{(1)}$—$O_{(2)}$ bond.

TABLE 3. Changes in π Atomic Occupancy Along the Reaction Coordinate I → III, Calculated by the MPDP Method

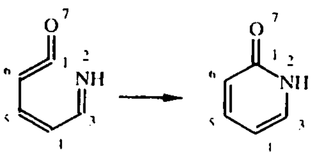
Structure	$C_{(1)}$	$O_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$O_{(7)}$
1	0,8621	1,34479	0,71291	1,15694	0,87275	1,36405	1,68328
2	0,86184	1,34533	0,71288	1,15745	0,87243	1,3652	1,68477
3	0,85432	1,3572	0,70846	1,16251	0,86915	1,36913	1,67938
4	0,84297	1,36387	0,70574	1,16965	0,85816	1,37511	1,66823
5	0,81675	1,40467	0,6925	1,20375	0,83436	1,40123	1,64674
6	0,78216	1,4723	0,6827	1,24892	0,80328	1,41252	1,59803
7	0,73934	1,62393	0,72036	1,29823	0,78708	1,35522	1,47568
8	0,75686	1,65969	0,741	1,26198	0,81783	1,31441	1,44817
9	0,78393	1,71516	0,81882	1,20496	0,86291	1,20611	1,40688
10	0,77627	1,78151	0,90895	1,139	0,8966	1,10817	1,38951

TABLE 4. Squares of the MO Coefficients in the Reaction I → III, Calculated by the MPDP Method

Structure	Orbitals (atom, number, orientation)		
	$O_{(2)}$-17, p_x	$C_{(1)}$-20, p_x	$O_{(7)}$-20, p_x
1	0,59770	0,62336	0,30010
2	0,58820	0,62440	0,30060
3	0,50498	0,62533	0,29612
4	0,47143	0,61627	0,28571
5	0,45630	0,61983	0,27112
6	0,42250	0,57710	0,23090
7	0,33597	0,00000	0,00000
8	0,25413	0,00000	0,00000
9	0,15294	0,00000	0,00000
10	0,12120	0,00000	0,00000

CYCLIZATION OF 1-AZA-1,3,5-HEXATRIENE (II) TO 2-PYRIDONE (IV)

In distinction from 1-oxabutadienylketene (I), 1-azabutadienylketene (II) has a hydrogen atom on the terminal heteroatom, the position of which in the transition state forces an unambiguous conclusion about the mechanism of formation of the new σ-bond:



II IV

The direction of the new $C_{(1)}$—$N_{(2)}$ bond was chosen as the reaction coordinate as done for ketene (I). In Tables 5-8 structure 1 corresponds to the reactant, structure 6 to the transition state and structure 10 to the final product. The calculated activation energy is 3.1 kcal/mol, which is approximately 6 kcal/mol lower than that for the 1-oxa analog. Such a value for E_{act} agrees with the larger availability of the nitrogen unshared pair for electrophilic attack by comparison with the oxygen atom.

The calculated data for the geometry and interplanar angles for the intermediate state, the initial and final structures are given in Table 5. The interplane angles [12, 13] $C_{(6)}$—$C_{(1)}$—N—H (H is the hydrogen atom attached to $C_{(3)}$) and N—$C_{(1)}$—$C_{(6)}$—H are close to 180° throughout the reaction, which is in complete agreement with mechanism (b). The characters of the changes in bond length, charges, π atom occupancy, and the squares of the AO in the boundary MO for the cyclization of 1-aza-1,3,5-hexatriene (II) are precisely the same as for the cyclization of 1-oxa-1,3,5-hexatriene (I) (see Tables 6-8).

TABLE 5. Geometric Parameters for the Reaction II → IV Obtained by the MPDP Method

Parameter	Structure										
	1	2	3	4	5	6	7	8	9	10	11
Bond Length, Å											
$C_{(1)}-N_{(2)}$	2,787	2,651	2,632	2,480	2,330	2,167	1,941	1,769	1,567	1,430	1,427
$O_{(2)}-C_{(3)}$	1,292	1,301	1,301	1,301	1,301	1,300	1,301	1,301	1,301	1,390	1,301
$C_{(3)}-C_{(4)}$	1,462	1,461	1,459	1,461	1,459	1,453	1,437	1,431	1,418	1,372	1,404
$C_{(4)}-C_{(5)}$	1,359	1,357	1,362	1,359	1,365	1,368	1,385	1,376	1,362	1,445	1,359
$C_{(5)}-C_{(6)}$	1,442	1,440	1,443	1,437	1,438	1,432	1,404	1,360	1,376	1,366	1,368
$C_{(6)}-C_{(1)}$	1,340	1,345	1,355	1,346	1,349	1,360	1,387	1,425	1,430	1,480	1,426
$C_{(1)}-O_{(7)}$	1,770	1,177	1,176	1,176	1,179	1,181	1,187	1,194	1,205	1,229	1,219
Bond Angle, deg											
$N_{(2)}-C_{(3)}-C_{(4)}$	122,70	120,98	122,20	122,87	120,48	119,60	119,51	119,33	119,01	120,70	118,52
$C_{(3)}-C_{(4)}-C_{(5)}$	131,20	130,63	127,32	126,14	124,99	123,90	123,53	123,21	122,62	119,60	121,92
$C_{(4)}-C_{(5)}-C_{(6)}$	133,00	131,71	131,96	130,84	129,08	127,80	125,72	125,28	124,44	120,30	123,55
$C_{(5)}-C_{(6)}-C_{(1)}$	130,00	129,47	132,62	130,01	130,74	128,90	124,49	120,85	115,32	121,60	112,95
$C_{(6)}-C_{(1)}-O_{(7)}$	174,40	172,87	174,45	171,26	166,11	162,30	148,29	150,90	142,67	117,30	134,82
E_{act}	22,71794	22,8415	23,60426	23,9185	25,08889	25,58089	23,14621	19,83885	13,10275	-7,0248	11,1167

TABLE 6. Changes in the Atomic Charges Along the Reaction Coordinate II → IV, Calculated by the MPDP Method

Structure	$C_{(1)}$	$N_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$O_{(7)}$
1	0,375	-0,294	0,111	-0,173	0,103	-0,297	-0,132
2	0,386	-0,306	0,115	-0,182	0,107	-0,302	-0,134
3	0,391	-0,311	0,116	-0,183	0,112	-0,302	-0,134
4	0,404	-0,322	0,122	-0,191	0,114	-0,311	-0,139
5	0,426	-0,329	0,129	-0,205	0,123	-0,318	-0,158
6	0,452	-0,352	0,153	-0,230	0,136	-0,333	-0,180
7	0,486	-0,378	0,200	-0,293	0,163	-0,347	-0,231
8	0,470	-0,380	0,203	-0,316	0,157	-0,304	-0,266
9	0,409	-0,328	0,181	-0,290	0,124	-0,253	-0,338
10	0,383	-0,339	0,128	-0,195	0,044	-0,167	-0,361
11	0,358	-0,277	0,145	-0,251	0,083	-0,200	-0,387

TABLE 7. Changes in π Atomic Occupancy Along the Reaction Coordinate II → IV, Calculated by the MPDP Method

Structure	$C_{(1)}$	$N_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$O_{(7)}$
1	0,86488	1,19269	0,85225	1,13668	0,89969	1,36155	1,69109
2	0,85661	1,20437	0,84547	1,1442	0,89438	1,36919	1,68548
3	0,85249	1,20918	0,84375	1,14675	0,89067	1,36814	1,67901
4	0,84584	1,22079	0,83692	1,15612	0,88456	1,37831	1,67689
5	0,83378	1,24147	0,82705	1,16821	1,16821	1,38486	1,67014
6	0,81438	1,27916	0,81051	1,19246	0,85509	1,39629	1,65209
7	0,74352	1,49242	0,7889	1,2848	0,82273	1,35492	1,51311
8	0,76454	1,57052	0,82151	1,25345	0,84457	1,27326	1,47087
9	0,78111	1,64629	0,90418	1,19169	0,87509	1,1492	1,45242
10	0,76577	1,70051	0,9243	1,14808	0,90226	1,11266	1,44642

TABLE 8. Squares of the MO Coefficients in the Reaction II → IV, Calculated by the MPDP Method

Structure	$N_{(2)}$-16, p_x	$C_{(1)}$-20, p_x	$O_{(7)}$-20, p_x
1	0,4562	0,6260	0,2950
2	0,4674	0,6280	0,2917
3	0,4665	0,6270	0,2875
4	0,4602	0,6267	0,2853
5	0,4435	0,6192	0,2720
6	0,4273	0,6016	0,2512
7	0,2608	0,0027	0,0008
8	0,0366	0,0007	0,0002
9	0,0000	0,0000	0,0000
10	0,1007	0,0000	0,0000

Thus the more rapid cyclization of 1-heterobutadienylketenes in comparison with butadienylketenes is explained on the basis of the above calculations as a result of a different heteroelectrocyclic mechanism (b), which does not require relative rotation of the terminal bonds of the 1,3,5-hexatriene system.

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