Model Theoretical Study of 2 + 2 Cycloadditions of Dialkoxyethynes with Heterocumulenes

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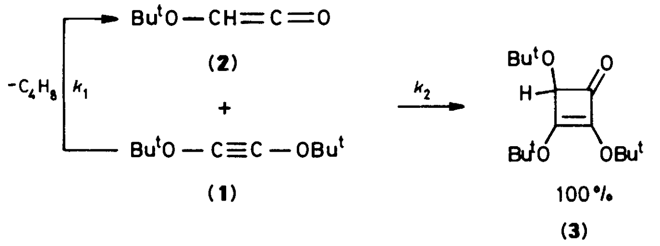
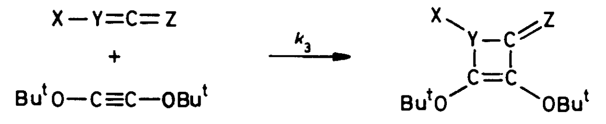
The 2 + 2 cycloaddition reactions of dihydroxyethyne (**4**), as a model for a dialkoxyalkyne, with hydroxyketene (**5**), isocyanic acid (**6**), formyl isocyanate (**7**), and isothiocyanic acid (**8**), as models for heterocumulenes, have been studied by the MNDO method. All the reactions are predicted to take place stepwise through very short-lived dipolar intermediates. Since MNDO tends to describe reactions as non-concerted due to overestimation of interatomic repulsions at distances around the van der Waals separation, these reactions can be properly classified as a borderline situation between a highly non-synchronous concerted mechanism and a stepwise one.

Di-t-butoxyethyne (**1**), the only acetylene diether kinetically stabilized towards thermal polymerization reported so far,[1] has proven to be a very useful synthon for the preparation of cyclic oxocarbons by means of thermal and metal-catalysed cycloaddition reactions.[2] The key step in some of these syntheses is a thermal 2 + 2 cycloaddition between (**1**) and t-butoxyketene (**2**) formed by thermal extrusion of 2-methylpropene from the acetylene diether, leading to 2,3,4-tri-t-butoxycyclobutenone (**3**) in quantitative yield[2a,b] (see Scheme 1). Since (**2**) is never detected as an intermediate during this reaction, its formation is assumed to be rate limiting, *i.e.* $k_2 > k_1$.



Scheme 1.

The formation of (**3**) takes place slowly at 30—40 °C, but rapidly (*ca.* 1 h) at 80 °C. Accordingly, the utilization of di-t-butoxyethyne in other cycloadditions that require thermal activation is precluded.



Scheme 2.

In the course of a study of the highly elusive azetin-2-ones and their thio-analogues, we planned to perform the reaction of (**1**) with a variety of alkyl and aryl isocyanates and isothiocyanates, as well as with acyl isocyanates.

Irrespective of the potential instability of the desired products,[3] the possibility of achieving their syntheses by means of the forementioned 2 + 2 cycloaddition reactions relies on the existence of a favourable balance between the activation energies of the processes leading to them and that of the cycloaddition process between (**1**) and (**2**). Thus, if $k_3 > k_2$, it could be expected that the reactions proceed without significant formation of (**2**) and, subsequently, of (**3**).

In order to clarify this basic question, we decided to perform a theoretical study on the 2 + 2 cycloadditions of dihydroxyethyne (**4**), taken as a model for compound (**1**), with hydroxyketene (**5**), isocyanic acid (**6**), formyl isocyanate (**7**), and isothiocyanic acid (**8**), as models for the forementioned heterocumulenes.

In this context, it is worth nothing that in spite of the synthetic interest of many 2 + 2 cycloadditions of acetylenes with heterocumulenes, little attention has been devoted to the study of their mechanisms, either from the experimental, or from the theoretical point of view. Thus, it is generally believed that due to the presence in each reacting species of two orthogonal π systems, the geometrical requirements for a concerted $2\pi_s + 2\pi_a$ mechanism can be easily accomplished but, in any case, there are no arguments for discarding the possibility of a polar stepwise mechanism.[4]

Calculations

The size of the molecular systems strongly recommended the use of a semiempirical, yet reliable, SCF MO method. MNDO was selected for the following reasons. (i) It is well stablished for the study of chemical reactions, usually leading to results comparable with those of high level *ab initio* calculations.[5] (ii) The MNDO-calculated heats of formation for systems comparable to those in our study like acetylene, allene, and cyclobutene, are in better agreement with the experimental values than those derived from *ab initio* SCF MO calculations.[6] (iii) The tendency of MNDO to overestimate activation energies relative to the experimental values is not relevant to our study since we are interested in comparing the activation energies for a series of similar reactions.

All calculations reported in the present paper were performed with the standard version of MNDO,[7] as implemented in the MOPAC package of programs.[8] The RHF version has been used throughout after testing and eliminating the existence of diradical character in all intermediates and transition states. Geometries for ground states have been determined by minimizing the energy with respect to all geometrical variables, using the DFP algorithm.[9] Transition states have been located either by the normal reaction co-ordinate method or with the NLLSQ algorithm,[10] refined by minimizing the gradient norm of the energy, and characterized by establishing that the Hessian (force constant) matrix had one, and only one, negative eigenvalue. The progress of the reactions were followed by means of the bond index B(A–B) between atoms A and B, defined by $B(\text{A–B}) = \Sigma_\lambda\Sigma_\sigma P^2_{\lambda\sigma}$ where $P_{\lambda\sigma}$ is an element of the bond-order matrix and where subscripts λ and σ refer to atomic orbitals centred at atoms A and B, respectively.

Results and Discussion

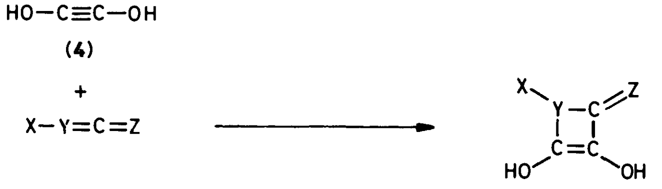
The possibility of a concerted synchronous mechanism was, in all cases, first investigated by defining a reaction co-ordinate as the distance between the central points of the C–C bond of the dihydroxyethyne fragment and the Y–C bond of the heterocumulene fragment in the cycloadducts. However, no single transition structure connecting product and reactants could be located in any case. On the other hand, all four cyclic products (**9**)—(**12**) exhibited a strong tendency for the preferential cleavage of one of the two bonds connecting the fragment molecules.

It must be realized that a particular ordering in bond cleavage does not necessarily mean the opposite one is preferred in the synthetic direction. Consequently, both possible orderings of bond formation were studied in all cases.

The processes by which the initial interaction takes place between dihydroxyethyne and the carbonyl (or thiocarbonyl) carbon atom in the heterocumulene are characterized by electronic transfer from (**4**) into the heterocumulene molecule [in terms of FMO theory we would say that the HOMO of (**4**) is interacting with the LUMO of heterocumulene] and are those expected to be preferred from qualitative considerations. In all four cases studied we have been able to determine a minimum-energy reaction path (m.e.r.p.) connecting reactants and product through a short-lived reaction intermediate according to this approach. In the subsequent discussion we will refer to this mode of reaction as path *a* (see Scheme 4).

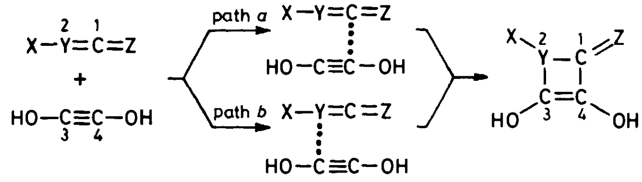
On the other hand, the processes by which the initial interaction takes place between dihydroxyethyne and the Y atom in the heterocumulene are characterized by electronic transfer from the heterocumulene into the dihydroxyethyne molecule [*i.e.*, there is a predominant interacton of the HOMO of the heterocumulene with the LUMO of (**4**)]. This possibility could, in principle, be facilitated in the case of isocyanates and isothiocyanates by the fact that the HOMOs of these species have mainly the character of a highly polarizable non-bonding electron pair on the nitrogen atom. In the subsequent discussion we will refer to this mode of reaction as path *b*. Although in all the four cases studied a first transition state was located, whose occupied molecular orbitals correlated well with those of the reactants, only for the reactions with formyl isocyanate (**7**) and isothiocyanic acid (**8**) could a complete m.e.r.p. be determined.

In the reactions of (**4**) with hydroxyketene (**5**) and isocyanic acid (**6**), geometrical relaxation of the first transition state led to another region of the energy hypersurface. The same was observed when the back-reactions from the cycloadducts were studied, but in this case the change of region on the energy hypersurface took place prior to any transition state (*i.e.*, later than the second transition state in the synthetic sense). All attempts carried out to localize the reaction intermediate and the second transition state of the cycloaddition process failed. Although a minimum and a saddle point could be characterized along the reaction paths obtained either from the first transition state or from the final product, their occupied molecular orbitals



(**5**) X = H, HO; Y = C; Z = O (**9**)
(**6**) X = H; Y = N; Z = O (**10**)
(**7**) X = OCH; Y = N; Z = O (**11**)
(**8**) X = H; Y = N; Z = S (**12**)

Scheme 3.



Scheme 4.

Table 1. Relevant data for cycloaddition between dihydroxyethyne (**4**) and hydroxyketene (**5**): *d* = distance; *a* = angle; *da* = dihedral angle; *q* = atomic charge; net *q*(**4**) = net charge on the dihydroxyethyne moiety: *B* = bond order

		Path *a*				
	Reactants	First TS	Intermediate	Second TS	Path *b* First TS	Product
ΔH_f/kcal mol^{-1}	−83.00	−55.48	−62.40	−61.46	−45.86	−141.75
d(1-2)/Å	1.336	1.359	1.428	1.478	1.397	1.575
d(2-3)/Å		3.272	3.054	2.879	1.892	1.554
d(3-4)/Å	1.193	1.265	1.455	1.459	1.275	1.376
d(1-4)/Å		1.980	1.474	1.443	3.298	1.502
a(321)/°					102.61	83.67
a(432)/°					117.63	96.51
a(214)/°		109.35	119.32	117.37		88.91
a(143)/°		110.95	125.29	121.15		92.88
da(3412)/°		77.71	19.96	2.90		1.22
da(4321)/°					89.49	1.18
q(1)	0.257	0.299	0.167	0.198	0.285	0.267
q(2)	−0.145	−0.227	−0.011	0.212	0.039	0.141
q(3)	−0.061	0.025	0.099	−0.033	−0.078	0.023
q(4)	−0.061	−0.019	0.069	−0.100	−0.156	−0.111
net *q*(**4**)		0.203	0.302	−0.139	−0.232	−0.100
B(1-2)	1.638	1.551	1.230	1.008	1.296	0.858
B(2-3)		0.017	0.067	0.039	0.335	0.908
B(3-4)	2.660	2.133	1.092	1.077	2.133	1.672
B(1-4)		0.243	1.040	1.156	0.127	0.913

Table 2. Relevant data for cycloaddition between dihydroxyethyne (**4**) and isocyanic acid (**6**): *d* = distance; *a* = angle; *da* = dihedral angle; *q* = atomic charge; net *q*(**4**) = net charge on the dihydroxyethyne moiety; *B* = bond order

		Path *a*				
	Reactants	First TS	Intermediate	Second TS	Path *b* First TS	Product
ΔH_f/kcal mol^{-1}	−41.55	−10.46	−17.68	−17.39	−13.65	−84.39
d(1-2)/Å	1.248	1.284	1.322	1.328	1.273	1.488
d(2-3)/Å		2.860	2.586	2.356	1.720	1.450
d(3-4)/Å	1.193	1.273	1.338	1.333	1.274	1.384
d(1-4)/Å		1.970	1.584	1.574	3.375	1.503
a(321)/°					127.94	87.07
a(432)/°					117.00	95.05
a(214)/°		98.75	105.85	102.06		88.70
a(143)/°		110.76	116.03	111.60		88.91
da(3412)/°		55.89	24.15	11.15		3.83
da(4321)/°					80.09	3.99
q(1)	0.363	0.384	0.295	0.312	0.380	0.348
q(2)	−0.346	−0.431	−0.536	−0.566	−0.273	−0.284
q(3)	−0.061	0.031	0.079	0.109	0.006	0.200
q(4)	−0.061	−0.007	0.228	0.208	−0.167	−0.175
net *q*(**4**)		0.230	0.607	0.598	−0.158	0.035
B(1-2)	1.795	1.648	1.502	1.445	1.603	0.875
B(2-3)		0.013	0.039	0.093	0.316	1.010
B(3-4)	2.660	2.066	1.643	1.680	2.141	1.596
B(1-4)		0.258	0.709	0.726	0.079	0.891

Table 3. Relevant data for cycloaddition between dihydroxyethyne (**4**) and formyl isocyanate (**7**): *d* = distance; *a* = angle; *da* = dihedral angle; *q* = atomic charge; net *q*(**4**) = net charge on the dihydroxyethyne moiety; *B* = bond order

		Path *a*			Path *b*			
	Reactants	First TS	Intermediate	Second TS	First TS	Intermediate	Second TS	Product
ΔH_f/kcal mol^{-1}	−80.44	−54.45	−54.75	−54.10	−46.91	−47.21	−42.66	−118.46
d(1-2)/Å	1.250	1.289	1.327	1.325	1.290	1.302	1.311	1.484
d(2-3)/Å		3.413	3.580	3.248	1.680	1.559	1.473	1.434
d(3-4)/Å	1.193	1.273	1.354	1.333	1.292	1.331	1.387	1.338
d(1-4)/Å		1.957	1.583	1.593	3.278	3.246	2.763	1.498
a(321)/°					118.33	117.56	112.74	88.72
a(432)/°					118.83	121.83	112.99	93.87
a(214)/°		111.43	107.57	105.41				87.49
a(143)/°		113.55	119.24	118.70				89.91
da(3412)/°		94.52	160.68	106.76				0.26
da(4321)/°					82.77	84.01	54.00	0.27
q(1)	0.451	0.472	0.344	0.334	0.450	0.459	0.494	0.433
q(2)	−0.451	−0.500	−0.581	−0.569	−0.332	−0.279	−0.207	−0.475
q(3)	−0.061	0.045	0.021	0.020	−0.043	−0.129	−0.236	0.316
q(4)	−0.061	−0.046	0.282	0.278	−0.159	−0.135	−0.187	−0.219
net *q*(**4**)		0.221	0.657	0.631	−0.219	−0.333	−0.515	0.128
B(1-2)	1.683	1.438	1.388	1.398	1.458	1.378	1.331	0.807
B(2-3)		0.036	0.019	0.015	0.380	0.565	0.787	0.982
B(3-4)	2.660	2.072	1.549	1.645	2.019	1.760	1.431	1.546
B(1-4)		0.245	0.728	0.691	0.074	0.081	0.032	0.895

did not correlate with those of the first transition state, and the negative eigenvalue for the saddle point corresponded to a loss of CO from the supermolecule.

We will discuss now the main features of the four cycloaddition processes according to both paths *a* and *b*. The numbering of atoms used in the discussion is indicated in Scheme 4. All relevant data for the reaction studied are summarized in Tables 1—4. Geometrical parameters for all stationary points in our study are given in cartesian coordinates in Supplementary Publication No. SUP 56654 (16 pp.).*

Cycloadditions between Dihydroxyethyne (**4**) *and Heterocumulenes* (**5**)—(**8**) *according to Path* a.—Computer-generated drawings for stationary points in path *a* for these reactions are given in Figures 1—4. A geometrical analysis indicates that in all the cases the reactants approach one another in a perpendicular orientation, leading exclusively to a two-centre interaction. Thus, in the first transition state there is practically no interaction between atoms Y(2) and C(3), as indicated by the very small (0.012—0.036) bond indices between them. In contrast, the formation of C(1)–C(4) bonds at this point is already advanced, as indicated by the relatively short (1.957—2.044 Å) C(1)–C(4) distances and the considerable bond indices (0.237—0.258). At this point, geometries of the heterocumulene fragments show only minor changes relative to the separated molecules, whereas the C(3)–C(4) triple bond in the dihydroxy-

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* For details of Supplementary Publications see Instructions for Authors in *J. Chem. Soc., Perkin Trans. 2*, 1987, Issue 1.

Table 4. Relevant data for cycloaddition between dihydroxyethyne (**4**) and isothiocyanic acid (**8**): *d* = distance; *a* = angle; *da* = dihedral angle; *q* = atomic charge; net *q*(**4**) = net charge on the dihydroxyethyne moiety; *B* = bond order

		Path *a*			Path *b*			
	Reactants	First TS	Intermediate	Second TS	First TS	Intermediate	Second TS	Product
ΔH_f/kcal mol^{-1}	7.59	37.50	20.16	23.30	37.76	35.99	36.48	−29.31
d(1-2)/Å	1.218	1.254	1.303	1.316	1.258	1.293	1.295	1.471
d(2-3)/Å		2.957	2.686	2.202	1.695	1.419	1.434	1.458
d(3-4)/Å	1.193	1.260	1.344	1.343	1.280	1.408	1.388	1.386
d(1-4)/Å		2.044	1.538	1.533	3.444	2.725	2.499	1.488
a(321)/°					124.83	123.33	118.01	87.37
a(432)/°					117.70	114.65	108.93	93.73
a(214)/°		97.32	110.33	99.93				89.11
a(143)/°		110.22	119.49	109.03				89.43
da(3412)/°		66.58	20.34	6.04				4.59
da(4321)/°					101.41	1.88	2.00	4.70
q(1)	0.203	0.233	0.104	0.145	0.152	0.029	0.114	0.138
q(2)	−0.313	−0.352	−0.391	−0.469	−0.203	0.001	−0.043	−0.238
q(3)	−0.061	0.010	0.047	0.112	−0.023	−0.181	−0.168	0.192
q(4)	−0.061	−0.005	0.313	0.253	−0.157	−0.130	−0.165	−0.144
net *q*(**4**)		0.202	0.704	0.658	−0.183	−0.391	−0.394	0.071
B(1-2)	2.076	1.927	1.743	1.628	1.797	1.529	1.541	0.969
B(2-3)		0.012	0.022	0.145	0.354	0.967	0.904	0.987
B(3-4)	2.660	2.159	1.591	1.640	2.093	1.298	1.397	1.569
B(1-4)		0.237	0.839	0.850	0.103	0.072	0.145	0.981

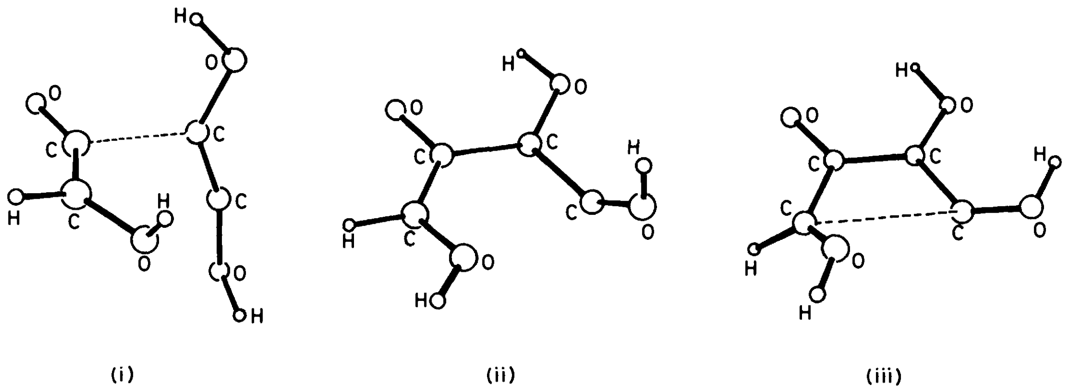


Figure 1. Computer-generated drawings for stationary points in path *a* of cycloaddition between dihydroxyethyne (**4**) and hydroxyketene (**5**): (i) first transition state, (ii) reaction intermediate, (iii) second transition state

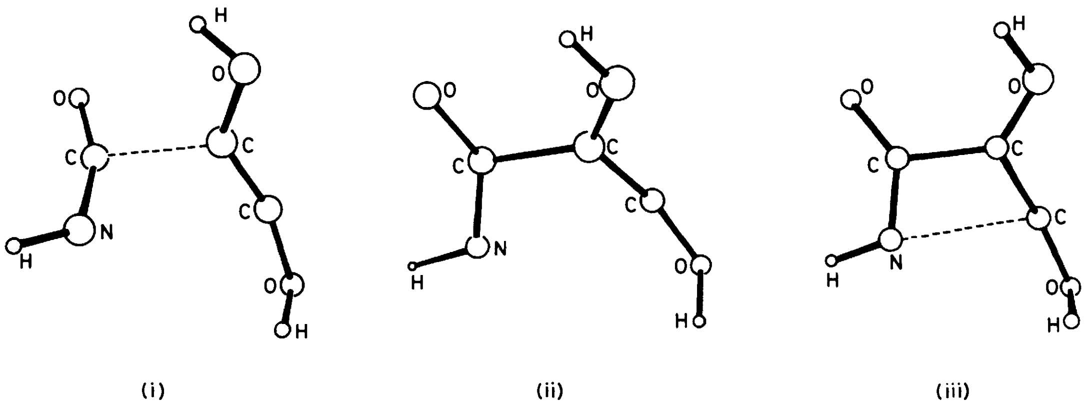
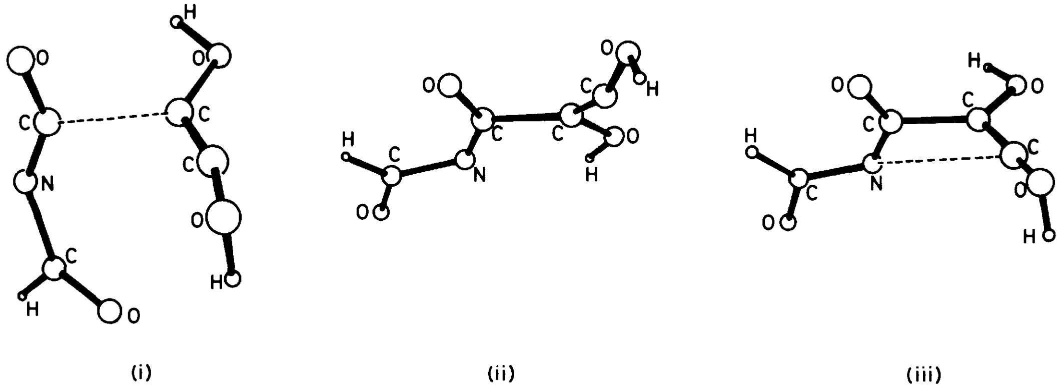
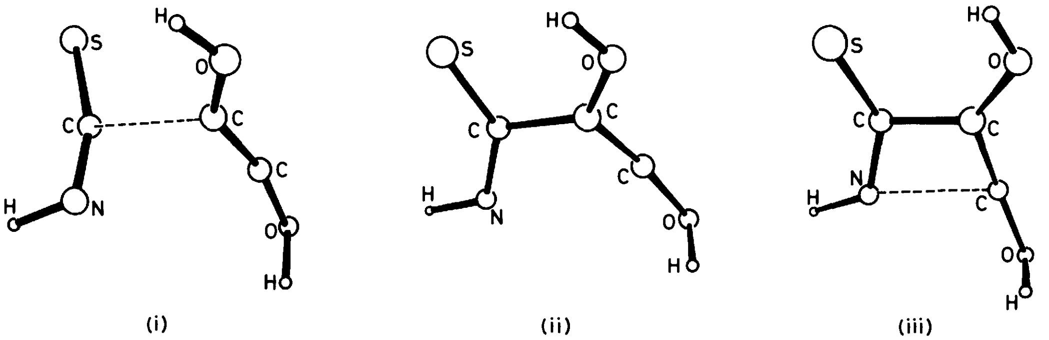


Figure 2. Computer-generated drawings for stationary points in path *a* of cycloaddition between dihydroxyethyne (**4**) and isocyanic acid (**6**): (i) first transition state, (ii) reaction intermediate, (iii) second transition state



(i) (ii) (iii)

Figure 3. Computer-generated drawings for stationary points in path *a* of cycloaddition between dihydroxyethyne (**4**) and formyl isocyanate (**7**): (i) first transition state, (ii) reaction intermediate, (iii) second transition state



(i) (ii) (iii)

Figure 4. Computer-generated drawings for stationary points in path *a* of cycloaddition between dihydroxyethyne (**4**) and isothiocyanic acid (**8**): (i) first transition state, (ii) reaction intermediate, (iii) second transition state

ethyne moiety of the supermolecules exhibits a considerable elongation.

Allowance for geometry relaxation in this transition state leads, in the four cases, to the reaction intermediate, with significant change in the C(1)–Y(2), C(3)–C(4), and C(4)–C(1) distances. The dihedral angles C(3)C(4)C(1)Y(2), which define the relative orientation of the fragment molecules, have diminished except in the reaction of (**4**) with formyl isocyanate (**7**) where the intermediate is almost antiperiplanar with a value for this dihedral angle of 160.7°. At this point, the interaction between Y(2) and C(3) is still weak.

Further rotation around the C(1)–C(4) bond leads to the transition state for the cyclization step without important changes in other geometrical parameters. Except in the reaction (**4**) + (**7**), a small rotation (14.2—17.1°) around the C(1)–C(4) bond in the intermediate is enough for initiating the cyclization process. It should be mentioned that these transition states are very early ones, occuring at Y(2)–C(3) distances of 3.248—2.202 Å when bond indices between these atoms are still small (0.015—0.145).

From the electronic point of view, in all cases the interaction between dihydroxyethyne (**4**) and heterocumulenes (**5**)—(**8**) according to path *a* is accompanied by an important electron-density transfer from the acetylene moiety into the heterocumulene one, as could be anticipated from simple qualitative considerations. This charge transfer reached a maximum value in the reaction intermediate (0.302—0.704) and the whole process can be represented as depicted as Figure 5.

Centring now our attention on the calculated energy profile for the reaction, MNDO predicts the existence of a very short-lived zwitterionic intermediate. If consideration is taken of the fact that MNDO tends to overestimate interatomic repulsions at distances around the van der Waals separation,[9] as is the case for the cyclization step, the reaction can be properly classified as a borderline situation between a highly non-synchronous concerted mechanism and a stepwise one.

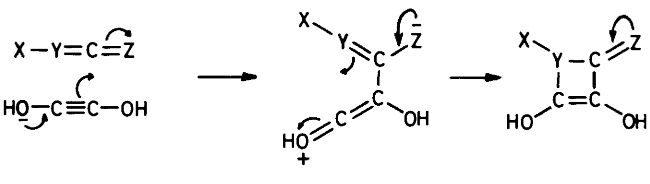


Figure 5. Representation of cycloaddition process between dihydroxyethyne (**4**) and heterocumulenes (**5**)—(**8**) according to path *a*

On comparing the three reactions in path *a* where the heterocumulene contains a nitrogen atom, *i.e.* (**4**) + isocyanic acid (**5**), (**4**) + formyl isocyanate (**6**), and (**4**) + isothiocyanic acid (**7**), some points can be made.

In (**4**) + (**6**) the main characteristic is the similarity in thermodynamic stability between the singular points along the minimum-energy reaction path. Thus, the first transition state, the reaction intermediate, and the second transition state lie in a range of 0.65 kcal mol^{-1} despite the important geometrical differences between them. From the geometric and electronic point of view, the stationary points resemble the corresponding ones in the cycloaddition with isocyanic acid. It appears, then, that the main effect derived from the introduction of a formyl substituent on the isocyanate moiety is that of making the reaction 'more concerted', but with a high degree of asymmetry in the bond-forming processes.

In (**4**) + (**7**) the main characteristic is the greater kinetic stability found for the reaction intermediate relative to the other cases. The main effect due to the presence of the sulphur atom in the heterocumulene moiety comes from the polarizability of the C(1)–S double bond. Thus, as the reaction proceeds, the C(1)–N(2) double bond is essentially conserved, indicating that the electron density coming from dihydroxyethyne is mainly fed into the π*C(1)–S orbital. This fact probably gives rise to the abnormally high barrier for the cyclization step, since the electron distribution of the reaction intermediate has to suffer considerable reorganization before cyclization can proceed.

Cycloadditions between Dihydroxyethyne (**4**) *and Heterocumulenes* (**5**)—(**8**) *according to Path* b.—From the geometrical point of view, the cycloadditions according to path *b* began with both reacting molecules approaching in a perpendicular orientation and bringing the Y(2) and C(3) atoms into bonding distance. The first transition states for such an interaction occur on the corresponding m.e.r.p.s in a very advanced stage, as indicated by the very short Y(2)–C(3) distances (1.680—1.892 Å) and the very high bond indices (0.380—0.316) between these atoms. With only the exception of the reaction between hydroxyketene (**5**) and dihydroxyethyne (**4**), the activation energies for the first step in cycloadditions according to path *b* are very similar to the corresponding ones calculated for path *a*. On the other hand, in the cycloadditions of the nitrogen-containing heterocumulenes (**6**)—(**8**), the C(1)–N(2) distance exhibits only minor changes in the transition state with respect to the isolated molecules, but the C(3)–C(4) bond in the dihydroxyethyne moiety is considerably elongated.

These facts can be easily interpreted by considering the highly polarizable lone pair on the nitrogen atom to be responsible for the creation of the new bond. In the cycloaddition with hydroxyketone (**5**), where the forementioned lone pair is lacking, the interaction between the reacting molecules is more energy consuming and provokes a deeper distortion in the molecular geometries of the interacting species.

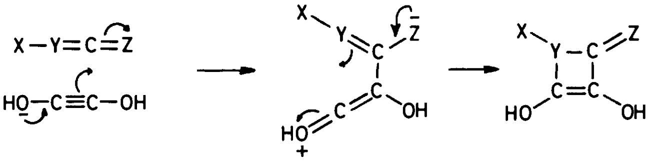


Figure 6. Representation of cycloaddition process between dihydroxyethyne (**4**) and nitrogen-containing heterocumulenes (**6**)—(**8**) according to path *b*

As already mentioned, only in the cycloadditions with formyl isocyanate (**7**) and isothiocyanic acid (**8**) has it been possible to determine a complete m.e.r.p. for path *b*. In these cases, from an electronic point of view, the cycloadditions are characterized by an important charge-density transfer from the heterocumulene into dihydroxyethyne in the initial stages of the reaction. The net charge on the acetylene fragment increases as the reaction proceeds, the charge distribution only adapting to that of the final product when the second transition state is already past. The whole process can be represented as depicted in Figure 6. Computer-generated drawings for the stationary points of the reaction between dihydroxyethyne (**4**) and formyl isocyanate (**7**) according to path *b* are given in Figure 7.

Character of the 2 + 2 *Cycloadditions of Dihydroxyethyne* (**4**) *with Heterocumulenes* (**5**)—(**8**).—All calculated activation energies and heats of reaction for the formation of reaction intermediates and final products from the starting molecules are summarized in Table 5. The rate-limiting step of the reactions is in some cases the first and in others the second. A more general characteristic is, however, the low value of the activation energy for the conversion of the reaction intermediate into the final product. It is known that the MNDO method tends to overestimate interatomic repulsions at distances around the van der Waals separation. Consequently, in transition states containing long weak bonds, as is the case for the second transition states of the reactions in our study, MNDO will tend to give a higher positive energy and hence too large an activation energy for the reaction.[11] In any case, the calculated activation energies are small and doubts arise on the nature, stepwise or concerted, of the reactions.

At this point, it is convenient to remember the distinction introduced by Dewar between two terms, synchronicity and concertedness, normally used as synonyms.[12] According to Dewar, a synchronous reaction is one where all the bond-making and bond-breaking processes take place in unison, having all proceeded to comparable extents in the transition state, whereas a concerted reaction is one that takes place in a single kinetic step, without necessarily being synchronous.

According to Woodward–Hoffmann rules, a 2π + 2π cycloaddition can only take place in a 'concerted' manner provided that a supra–antara interaction occurs.[13] In this context, the term 'concerted' is used with the connotation of 'synchronous', and this is a fundamental question in all the formulations of the Woodward–Hoffmann rules.

According to our calculations, the interaction between dihydroxyethyne and heterocumulenes does not take place in an antarafacial manner. The reactions are predicted to be highly non-synchronous, but probably kinetically concerted.

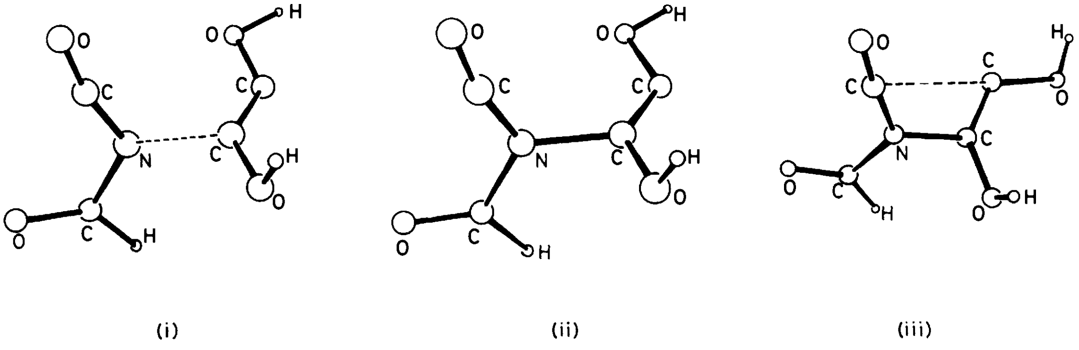
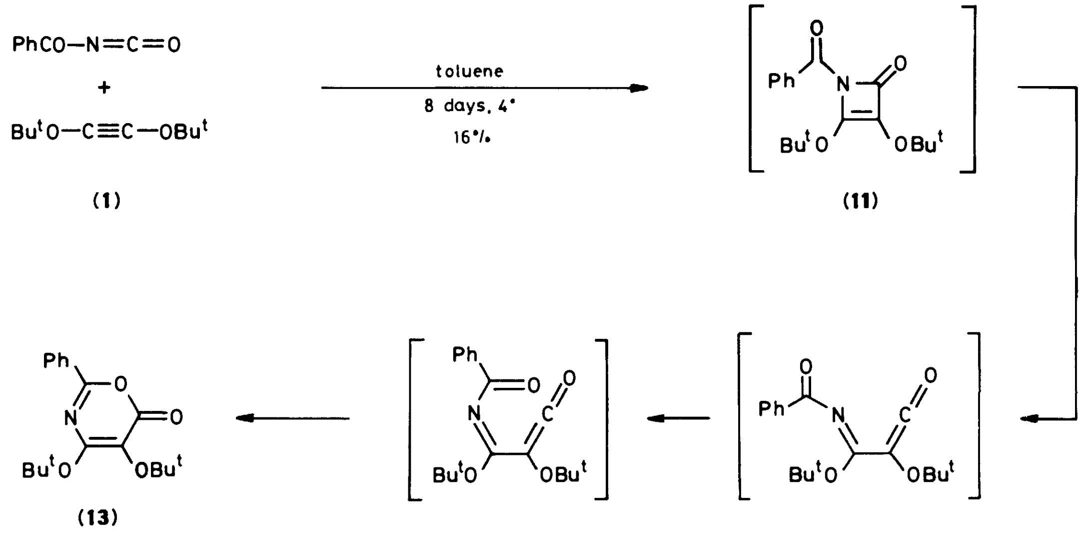


Figure 7. Computer-generated drawings for stationary points in path *b* of cycloaddition between dihydroxyethyne (**4**) and formyl isocyanate (**7**): (i) first transition state, (ii) reaction intermediate, (iii) second transition state



Scheme 5.

Table 5. Calculated activation energies for the first, $\Delta H_1^{\ddagger}$, and second, $\Delta H_2^{\ddagger}$, steps, and heats of reaction for the formation of reaction intermediates, ΔH_r (int.), and final products, ΔH_r (prod.), from the starting molecules for the cycloadditions between dihydroxyethyne (**4**) and heterocumulenes (**5**)—(**8**). All values are expressed in kcal mol^{-1}

Hetero-cumulene	Path	$\Delta H_1^{\ddagger}$	ΔH_r (int.)	$\Delta H_2^{\ddagger}$	ΔH_r (prod.)
(**5**)	*a*	27.52	20.60	0.94	−58.75
	b	37.14			
(**6**)	*a*	31.09	23.87	0.29	−42.84
	b	27.90			
(**7**)	*a*	25.99	25.69	0.65	−38.02
	b	33.53	33.23	4.55	
(**8**)	*a*	29.91	12.57	3.14	−36.90
	b	30.17	28.40	0.49	

It appears, thus, that, at least in these cases, the forbiddenness of concerted $2\pi + 2\pi$ cycloadditions could be essentially overcome by the way of non-synchronicity in the bond-forming processes implied in the reaction.

It should be mentioned here that our results are very similar to those recently reported by Burke for the cycloaddition of ketene with ethylene.[14] This author, using an *ab initio* treatment with extensive configuration interaction, has found the reaction to be a highly non-synchronous, concerted one with important charge separation, and he concluded that the $2\pi_s + 2\pi_s$ approach is not symmetry forbidden. He also found that the apparent antarafacial addition of ketene can be explained through electrostatic interactions during the initial stages of the approach.

It is worth noting that our results and those of Burke open an alternative way for the interpretation of the stereochemical courses of 2 + 2 cycloadditions of ketenes, which have normally been explained as the result of a concerted antarafacial addition.

Reactivity of Dihydroxyethyne (**4**) *towards Heterocumulenes* (**5**)—(**8**). *Chemical Derivations of the Model Theoretical Study.*—As can be seen in Table 5, in cases where both paths *a* and *b* have been completely determined, path *a* turns out to be preferred. This result is consistent with qualitative predictions that would attribute to dihydroxyethyne (**4**) the role of nucleophile and the role of electrophile to the heterocumulene.

In any case it should be noted that the difference in overall activation energy between paths *a* and *b* is very small in the reaction with isothiocyanic acid (**8**), seems to be small in the reaction with isocyanic acid (**6**), and only in the reactions with formyl isocyanate (**7**) and hydroxyketene (**5**) does it have an appreciable value. This fact correlates well with the diminution of the nucleophilic character of the atom in the heterocumulene which initiates the attack according to path *b*. According to path *a*, the predicted order of reactivity is: formyl isocyanate > hydroxyketene > isothiocyanic acid > isocyanic acid.

Translating the results of this model study into the laboratory practice, we attempted the 2 + 2 cycloadditions of di-t-butoxyethyne (**1**) with methyl, phenyl, and benzyl isocyanates, methyl, phenyl, and benzyl isothiocyanates, and with benzoyl isocyanate.

No 2 + 2 cycloaddition product other than 2,3,4-tri-t-butoxycyclobutenone (**3**) could be detected with the first six heterocumulenes cited. On the other hand, the reaction with benzoyl isocyanate proceeded well, even at low temperature, allowing the isolation of 4,5-di-t-butoxy-2-phenyl-6*H*-1,3-oxazin-6-one (**13**) without significant formation of cyclobutenone (**3**). The formation of (**13**) can only be explained through the intermediacy of *N*-benzoyl-3,4-di-t-butoxyazet-2(1*H*)-one (**11**) *via* an iminoketene intermediate (see Scheme 5). This conversion has been also indicated by MNDO calculations.[15]

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