

Can Heteroatoms Induce Violations of Orbital Symmetry Control? Electrocyclic Ring Opening of Oxirane†

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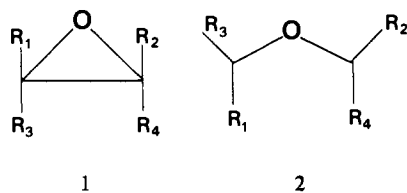
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Abstract: Electrocyclic ring opening at the C-C bond in oxirane is studied in a SCF+CI framework. A first approach of the potential energy surface is made by minimal (STO-3G) basis set calculations followed by limited configuration interaction (CI). The main reaction paths are then recomputed with an extended 4-31G basis set and extensive CI calculations using the CIPSI algorithm. Up to 700 000 determinants are included in these CI calculations. The following was shown: (i) Orbital symmetry rules control the thermal ring opening of unsubstituted oxirane molecule, the easiest reaction path being the conrotatory ring opening. The energy difference between conrotatory and disrotatory paths is rather low (10.9 kcal/mol), due to the somewhat high diradical character of carbonyl ylide intermediate. (ii) The best way to perform the cis-trans isomerization in oxirane involves first a conrotatory ring opening followed by a rotational isomerization of the carbonyl ylide which finally recloses in a conrotatory manner. The highest point on this reaction path is the transition state for rotational isomerization in carbonyl ylide. (iii) In agreement with experimental results, no loss of stereoselectivity can be expected in the ring opening process when the carbonyl ylide is free of steric constraints. However, experimental results by Huisgen and colleagues have also shown a loss of stereoselectivity in some substituted oxirane molecules. Our study suggests that these results come most likely from a rapid rotational isomerization in the intermediate carbonyl ylide rather than from a direct competition between the disrotatory and conrotatory paths.

According to the principle of conservation of orbital symmetry,¹ the electrocyclic ring opening of cyclopropyl anion to allyl anion should be conrotatory in a thermal reaction and disrotatory in a photochemical reaction. A large number of experimental studies have been undertaken to verify these predictions, in particular with neutral species isoelectronic with the cyclopropyl anion, i.e., aziridine and oxirane compounds. The C-C electrocyclic ring opening of these heterocycles leads to hetero analogues of the allyl anion, the azomethine and carbonyl ylides, respectively.

In 1967, the first experimental verification of the Woodward and Hoffmann predictions for the cyclopropyl anion was made by Huisgen and colleagues, who studied the electrocyclic ring opening of substituted aziridine molecules.² In these experiments, the ring-opened product is trapped with a dipolarophile by a concerted cycloaddition leading to a five-membered cycloadduct. Analysis of the cycloadduct structure has shown that the ring opening reaction was highly stereospecific, the steric course being precisely that allowed by symmetry orbital control: conrotatory and disrotatory for thermal and photochemical reactions, respectively.²

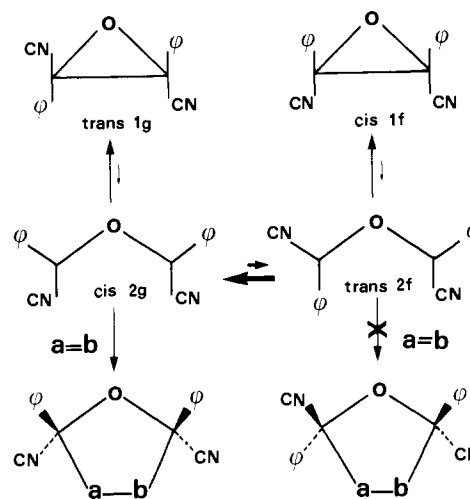
Later, the same kind of experiments have been made on iso-electronic oxirane molecules (1). First, Linn and Benson³ have



- 1
2
- $R_1 = R_2 = R_3 = R_4 = \text{CN}$
 - $R_1 = R_4 = \text{H}, R_2 = R_3 = \text{Ph}$
 - $R_1 = R_2 = \text{H}, R_3 = R_4 = \text{Ph}$
 - $R_1 = R_4 = \text{H}, R_2 = \text{Ph}, R_3 = \text{Ar}$
 - $R_1 = R_2 = \text{H}, R_3 = \text{Ar}, R_4 = \text{Ph}$
 - $R_1 = R_2 = \text{Ph}, R_3 = R_4 = \text{CN}$
 - $R_1 = R_4 = \text{CN}, R_2 = R_3 = \text{Ph}$
 - $R_1 = \text{H}, R_2 = R_3 = \text{Ph}, R_4 = \text{CN}$
 - $R_1 = \text{H}, R_2 = \text{CN}, R_3 = R_4 = \text{Ph}$
 - $R_1 = R_4 = \text{H}, R_2 = R_3 = 2\text{-Naph}$
 - $R_1 = R_2 = \text{H}, R_3 = R_4 = 2\text{-Naph}$

shown that tetracyanoethylene oxide (1a) can add at high tem-

Scheme I



perature to olefins, acetylenes, and aromatics, after breaking of the C-C bond. An intermediate structure, known today to be the carbonyl ylide (2), adds to the unsaturated molecules by a concerted or near-concerted cycloaddition.⁴ However, the substitution pattern in 1a precluded a conclusion about the ring opening stereochemistry. In 1970, Griffin and colleagues⁵ showed that in the photochemical ring opening of *trans*- and *cis*-stilbene oxides, 1b and 1c, respectively, a disrotatory course was involved (1c → 2b and 1b → 2c), a result in agreement with the orbital symmetry rules. In 1972, MacDonald and Crawford⁶ studied the kinetics of thermal racemization and cis-trans isomerization of *trans*- (1d) and *cis*-2-phenyl-3-*p*-tolylloxirane (1e). The slower rate of racemization of the *cis* isomer compared with that of the *trans* is

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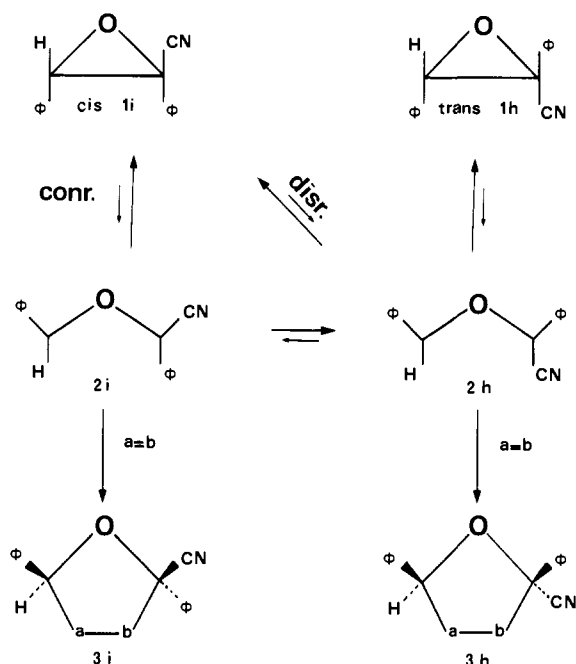
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† This work has been presented in part at the 13th Congress of Theoretical Chemists of Latin Expression, in Alghero (Sardinia), in October 1982.

Scheme II



consistent with a mechanism involving a thermal conrotatory ring opening of oxirane (**1d** → **2d** and **1e** → **2e**), a result again in agreement with the Woodward-Hoffmann rules.

However, a series of experiments by Huisgen and colleagues have clearly demonstrated that the agreement between theory and experiment may be altered by the substitution pattern of the starting molecule. First of all, Hamberger and Huisgen⁷ studied the C-C ring opening of *cis*- and *trans*-2,3-dicyano-2,3-diphenyloxirane (**1f** and **1g**, respectively) and their cycloaddition with dipolarophiles. Surprisingly, the same cycloadduct is obtained, whatever the starting oxirane isomer. If one still makes the assumption of an initial conrotatory ring opening of oxirane, one must admit that isomerization of the *trans*-dicyano-substituted carbonyl ylide (**2f**) to the more stable *cis* form (**2g**) precedes the 1,3-dipolar cycloaddition (Scheme I). This interpretation has been questioned after the study of electrocyclic ring opening of α -cyano-*trans*- and *cis*-stilbene oxide, **1h** and **1i**, respectively⁸⁻¹¹ (Scheme II). While the *trans* compound **1h** still leads, after cycloaddition with a dipolarophile, to the cycloadduct **3h**, consistent with an initial conrotatory ring opening (**1h** → **2h**), a mixture of "allowed" (42%) and "forbidden" (53%) cycloadducts is obtained from the *cis* compound **1i**.⁸ Furthermore, if the concentration of the dipolarophile is extrapolated to infinity, a situation which should prevent a *cis*-*trans* isomerization occurring in the carbonyl ylide intermediate (**2i** → **2h**) before the cycloaddition reaction, one should get 36% of the unexpected forbidden cycloadduct. Obviously, steric factors are responsible for the loss of stereospecificity in the ring opening reaction, since reactions leading to carbonyl ylide free of steric constraints (**1g** → **2g** and **1h** → **2h**) are totally stereospecific and lead to the expected allowed cycloadduct. The main question is then *what is the reaction path which can become competitive with the "normal" conrotatory ring opening mechanism?* Huisgen and Markowski¹⁰ suggested four possibilities to rationalize their results. Among them, the two more likely seem to be (Scheme II) the following: (a) The barrier for the conrotatory ring opening **1i** → **2i** would be higher than that

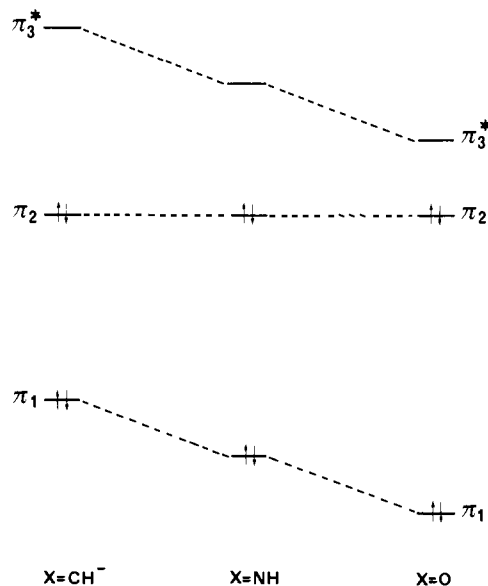


Figure 1. Schematic evolution, according to simple Hückel calculations, of the π orbital levels in $\text{CH}_2\text{-X-CH}_2$ species, with $\text{X} = \text{CH}^-$, NH , and O .

for *cis*-*trans* isomerization **2i** → **2h**. Then it would be possible that 36% of the molecule **2i** isomerize to the more favored *exo,exo* carbonyl ylide **2h**, because they would have enough rotational energy to pass the rotational barrier. (b) A direct *disrotatory* ring opening **1i** → **2h** (Scheme II) of the *cis* compound would be competitive with the conrotatory process ($\Delta E = 0.5$ kcal/mol). Therefore, both **2h** and **2i** carbonyl ylides would be formed directly from **1i**, leading to mixture of cycloadducts **3h** and **3i** after cycloaddition. This latter hypothesis, involving the participation of the forbidden disrotatory pathway, is thought by Huisgen to be the most probable.¹¹

Reasons why the disrotatory process could become competitive with the conrotatory one could be the following: (a) The Woodward-Hoffmann rules might not apply in a straightforward fashion in hetero three-membered rings. CNDO results by Schilling and Snyder¹² have already suggested that these rules have to be applied with caution in perturbed systems. (b) In the case of oxirane type molecules, Huisgen¹¹ pointed out that the rather high diradical character of carbonyl ylide should reduce the energy gap between conrotatory and disrotatory processes. Indeed, simple Hückel calculations readily show that the two π frontier orbitals (π_2 and π_3^* , Figure 1) are closer to each other in the open-chain structures $\text{CH}_2\text{-X-CH}_2$ as the electronegativity of the central atom increases ($\text{X} = \text{CH}^-$, NH , O). Therefore, the singlet ground state of carbonyl ylide species would contain a rather high percentage of doubly excited configuration ($\dots \pi_1^2 \pi_2^0 \pi_3^{*2}$), thus making the disrotatory pathway less forbidden.¹¹ However, the same argument leads one to predict a rather low rotational barrier around the C-O bond, a factor favoring a rapid *cis*-*trans* isomerization in carbonyl ylide.

Note finally that in a recent work by Griffin and colleagues,¹³ it is shown that both **1j** and **1k** lead to the same cycloadduct, a result which can also be rationalized either by a rapid isomerization from **2k** to the more stable **2j** structure or by a direct disrotatory ring opening **1k** → **2j**.

From these experimental recalls, one can conclude that a better understanding of the reaction mechanisms requires a knowledge of the relative activation energies for the following processes: conrotatory and disrotatory ring openings, rotational isomerization of carbonyl ylide, and perhaps nonconcerted ring opening of oxirane. The purpose of this paper is to study in detail these pathways for the oxirane molecule itself. It is our hope that a

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Table I. Relative Weights (in %) of Diradical and Zwitterionic Structures in the Wave Function of Planar Carbonyl Ylide (EE) Depending on the Type of Calculations

	$\dot{C}-O-\dot{C}$	$C=\dot{O}-\dot{C}$	$\dot{C}-\dot{O}=C$	$\dot{C}-O-\dot{C}$	$\dot{C}-O-\dot{C}$
SCF ^a	24	21.3	21.3	12	12
SCF + (2 × 2) CI ^{a,b}	59.2	16.2	16.2	1	1
SCF + (6 × 6) CI ^{a,c}	55.2	19.7	19.7	1.5	1.5

^a STO-3G closed-shell calculation, with C-O = 1.342 Å, ∠COC = 120° and C-H = 1.08 Å (ref 20). ^b CI between the ground and the first doubly excited configurations. ^c CI involving single and double excitations from the two occupied (π_1 and π_2) to the unoccupied (π^*_3) molecular orbitals.

detailed picture of the potential energy surface associated with the parent unsubstituted molecule can be an useful guide for interpreting the results in the substituted cases.

Method of Calculations

The formation of carbonyl ylide from oxirane¹⁴⁻¹⁷ as well as its addition to olefins¹⁸ have already been studied by ab initio calculations. One major conclusion of these studies is the rather high diradical character ($\dot{C}H_2-O-\dot{C}H_2$) of the carbonyl ylide species, calculated to be 38% by Hayes and Siu,¹⁹ 50% by Yamaguchi,²⁰ and 55% by Hiberty and Leforestier.²¹ Therefore, simple SCF calculations cannot give a correct description of these species, and a configuration interaction (CI) calculation is necessary to optimize the percentages of diradical and zwitterionic terms in the wave function²² (see Table I). Also, the transition states for conrotatory and disrotatory ring openings are likely to be structures in which the C-C bond is almost entirely broken, a case which is well-known to be badly described by simple SCF calculations. Therefore, it is clear that an investigation of the potential energy surface has to be done in a SCF + CI framework.

In a previous paper,²³ we have shown that a limited 3 × 3 CI calculation involving the three singlet configurations built from the two frontier orbitals was sufficient to correct the major defect of the simple SCF wave function (Table I) and leads to a rotational energy barrier in carbonyl ylide qualitatively in agreement with the value got from larger CI calculations.²³ Therefore, we decided to study the potential energy surface in the following manner: (i) calculations, involving optimizations of the various geometrical parameters, are first performed at the STO-3G²⁴ + (3 × 3) CI level to achieve a *qualitatively* proper description of open-chain structures (method I). (ii) In order to get *quantitatively* reliable values for the various energy barriers, the reaction paths optimized with method I are recomputed with the extended 4-31G basis set,²⁵ the SCF calculation being followed by an extensive CI calculation (method II). These CI calculations are carried out through the CIPSI²⁶ algorithm. A variational zero-order wave function is built by including all the determinants with coefficients larger

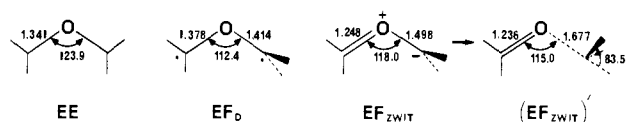


Figure 2. Main geometrical parameters characterizing the structures EE and EF (see the text).

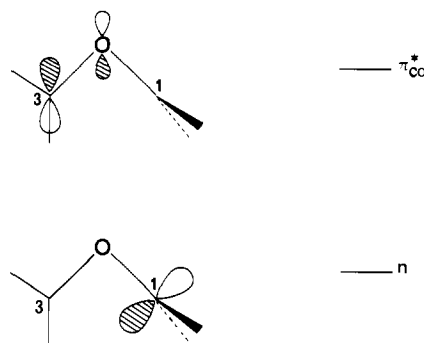


Figure 3. Shapes of the frontier molecular orbitals in EF structure.

than 0.03. The effects of the other determinants, generated by single and double excitations from the main determinants, are treated through a second-order perturbation. Depending on the points on the potential energy surface, the number of main determinants varies from 12 to 17, while the number of generated determinants is between 5×10^5 and 7×10^5 . We have verified that the value of 0.03 chosen for the selection of the main determinants was sufficiently low to avoid the defects of a poor convergence. For the SCF calculations, the GAUSSIAN 70 series of programs²⁷ were used. Both closed-shell and open-shell RHF²⁸ calculations were performed, and the calculation giving the lowest energy was retained. In general, open-shell calculations are slightly better for ring opened structures.

Results

Rotational Energy Barrier in Carbonyl Ylide²³ (Figures 4a and 5). We first studied the rotational isomerization in carbonyl ylide, i.e., the energy difference between the ground singlet states of the planar edge-to-edge (EE) structure and the edge-to-face (EF) structure in which one methylene group lies in the plane of the heavy atoms, the other being orthogonal to it. In these calculations, the C-O bond length and the COC and HCH angles are optimized, the methylene groups being assumed to be planar and the C-H bonds kept at 1.08 Å.

(a) Edge-to-Edge Structure (EE). Calculations of type I give the following optimized parameters: C-O = 1.341 Å, ∠COC = 123.9°, ∠HCH = 122.8° (Figure 2). The energy is then -150.8534 au. This value is lowered to -152.8791 au in calculations of type II, the geometry being that optimized with method I.

(b) Edge-to-Face Structure (EF). As was pointed out in a previous paper,²³ this structure has the electronic properties of a heterosymmetric diradical.²² In Figure 3 are schematically drawn the two frontier molecular orbitals of EF. The first one is a nonbonding orbital (n), lying in the plane of the heavy atoms, and located on the CH₂ group orthogonal to this plane. The second one, higher in energy, is a π^*_{CO} orbital, antibonding between the oxygen atom and C₃ (Figure 3). We have to put two electrons in these orbitals, with opposite spin if we restrict ourselves to the singlet configurations. Putting two electrons in the lowest energy orbital (n) leads to the (... n²) configuration, which can be represented approximately by the oxonium ylide structure EF_{zwitterion} (Figure 2). This structure has already been optimized at the STO-3G level.¹⁴ On the other hand, if one electron is put in each

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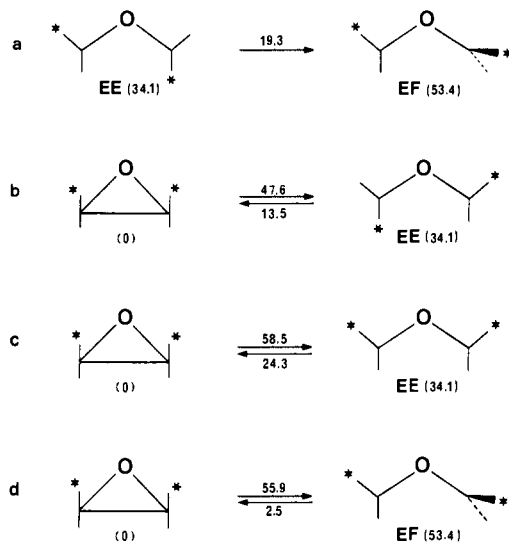


Figure 4. Computed energy barriers (in kilocalories per mole) for the various reaction paths by using calculations of type II: (a) rotational isomerization in carbonyl ylide; (b) conrotatory ring opening; (c) disrotatory ring opening; (d) nonsynchronous ring opening. The energy of oxirane has been calculated by using the geometry reported in ref 33. Energies of oxirane are -150.9285 (I) and -152.9335 au (II).

of the frontier orbitals, one gets the $^1n\pi^*$ configuration in which the electron in the n orbital is localized on C_1 , while the electron in π^*_{CO} orbital is mainly on C_3 because of the relative sizes of the coefficients in π^*_{CO} (Figure 3). The $^1n\pi^*$ configuration can be approximately described by the diradical structure EF_D (Figure 2). Our calculations show that the diradical state is the ground singlet state of EF, even if we take into account the larger stabilization occurring in EF_{zwit} if the CH_2 group carrying the minus charge is allowed to pyramidalize [$EF_{zwit} \rightarrow (EF_{zwit})'$, Figure 2]. In fact, the fully optimized structure $(EF_{zwit})'$ looks like a complex between carbene and formaldehyde and is more likely to be a precursor for the decomposition of oxirane than a transition state for rotational isomerization in carbonyl ylide.

In calculations of type I, the energy gap between EF_D and $(EF_{zwit})'$ is 46.9 kcal/mol, a difference which reduces to 20 kcal/mol in calculations of type II. The energy of EF_D is -150.8325 and -152.8484 au in calculations I and II, respectively. In the following, the notation EF will always correspond to the lowest singlet state of the edge-to-face structure, i.e., EF_D .

(c) Rotational Barrier in Carbonyl Ylide (Figures 4a and 5). The barrier for CO rotation in planar carbonyl ylide EE is computed to be 13.1 and 19.3 kcal/mol by calculations of type I and II, respectively. The latter value, which is the more reliable since the correlation effect is much better taken into account, is almost twice the value found by Yamaguchi (10 kcal/mol) using the PUHF 6-31G** method.²⁹ This difference is not surprising: recent calculations on methylene peroxide (CH_2COO) have also shown an increase of rotational energy barrier when the correlation effect is taken into account: the barrier increases from 11.2 (PUHF calculations)³⁰ to 19.1 by the GVB CI method³¹ and 21.7 kcal/mol by the multireference CI method.³⁰

Finally, in order to check our method of calculations (geometries optimized with method I used for calculations of type II), we have reoptimized the COC angle in EE and EF structures using method II. In both structures, the optimized angle value increases by 4° but the energy barrier between EE and EF remains equal to 19.3 kcal/mol.

Conrotatory and Disrotatory Ring Opening (Figures 4b,c and 5). The potential energy surfaces associated with conrotatory

and disrotatory ring opening of oxirane have been studied in the following manner: the COC angle (α) and the rotation angles of the methylene groups ($\theta = \theta_1 = \theta_3$ and $\theta = \theta_1 = -\theta_3$ for conrotatory and disrotatory paths, respectively) are treated as independent variables. α is varied from 90° to 150° by steps of 10° ; θ is varied from 90° (face-to-face) to 0° (edge-to-edge) by steps of 15° . At each point, the CO bond length and the HCH angles are optimized, the CH_2 groups being kept trigonal. We did not study COC angles smaller than 90° because it is known that in three-membered rings the rotation of terminal groups cannot occur before a sufficient bond stretching is achieved.³² Therefore, we get for each ring opening process a two-dimensional potential energy surface (α, θ) giving the reaction path and the transition-state structure.

(a) Conrotatory Ring Opening (Figures 4b and 5). With type I calculations, the transition-state geometry for the conrotatory pathway is characterized by the following parameters: $\angle COC = 100^\circ$, $\theta = 54^\circ$, $C-O = 1.397$ Å, and $\angle HCH = 119.6^\circ$. Recomputing the reaction path with type II calculations entails only a slight displacement of the transition state ($\theta = 58^\circ$ instead of 54°). The computed transition-state energies are -150.8396 (I) and -152.8576 au (II). The barrier for conrotatory oxirane ring opening (Figure 4) is 55.8 (I) and 47.6 kcal/mol (II) depending on the type of calculations, and the barrier for the conrotatory reclosure of carbonyl ylide is 8.7 (I) and 13.5 kcal/mol (II). Again, the values given by calculations of type II are expected to be more reliable (Figures 4b and 5).

(b) Disrotatory Ring Opening (Figures 4c and 5). With type I calculations the highest energy point for this path corresponds to the following set of parameters: $\angle COC = 108^\circ$, $\theta = 60^\circ$, $C-O = 1.408$ Å, and $\angle HCH = 120.6^\circ$. With type II calculations, the position of this point remains almost unchanged ($\theta = 59^\circ$). The computed energies are -150.8186 (I) and -152.8403 au (II), leading to barriers of 69.0 (I) and 58.5 kcal/mol (II) for the disrotatory ring opening of oxirane and, for the reverse reaction, to barriers of 21.8 (I) and 24.3 kcal/mol (II) (Figures 4c and 5). According to the most sophisticated calculations (II) the computed energy gap between conrotatory and disrotatory paths is 10.9 kcal/mol, a rather low value consistent with the diradical character of carbonyl ylide (Table I). Note, however, that the highest point on the disrotatory reaction path is *not actually a transition state*. Further calculations have shown that, starting from this point, the energy decreases not only along the reaction coordinate (disrotatory motion of the CH_2 groups) but also along a conrotatory motion of these groups. Therefore, this structure does not have the properties of a transition state since it is located at the top of a hill in the full multidimensional potential energy surface, at a point where the destabilizing electronic factors are maximized. This result is in agreement with previous calculations by Dewar and Kirschner³⁴ on forbidden electrocyclic reactions. These authors first showed that releasing the constraint of synchronous rotation of the methylene groups decreases the computed activation energy for the forbidden reaction. In particular, successive rotations of the two groups were found more favorable than synchronous rotation in the forbidden direction.

Nonsynchronous Ring Opening (Figure 4d). Finally, we have studied the nonsynchronous mechanism leading from oxirane to edge-to-face (EF) structure (Figure 4d). In this mechanism, only one methylene group is allowed to rotate, the other being kept orthogonal to the COC plane. Such a mechanism could play a role in the cis-trans isomerization of oxirane (direct reaction path avoiding the intermediate formation of planar carbonyl ylide), as well as in the loss of stereospecificity of the ring opening reaction.

The calculations have been performed in the way defined in the preceding section. The most important result is that the energy

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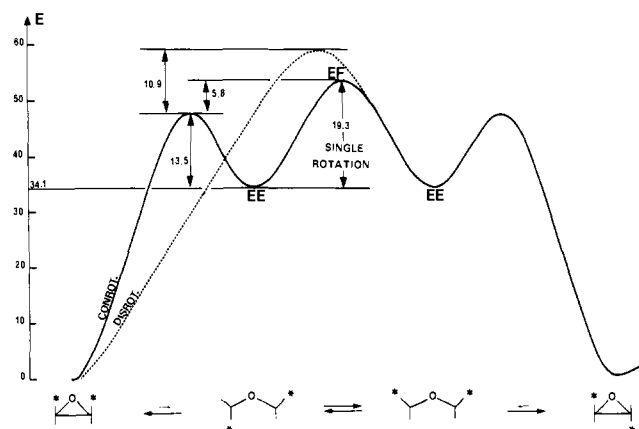


Figure 5. Energy profile for cis-trans isomerization of oxirane through the intermediate formation of planar carbonyl ylide (EE). The energy profile for disrotatory ring opening is also drawn (dotted lines). The energies are in kilocalories per mole. This figure can be compared with the experimental free energy profiles reported in ref 11 (Figures 3 and 5) and 6 (Figure 2).

barrier between oxirane and EF is higher than the energy difference between these structures (55.9 instead of 53.4 kcal/mol with method II). Consequently, the best way to form the EF structure from oxirane is the *indirect pathway* involving the intermediate formation of planar carbonyl ylide EE (oxirane $\xrightarrow{4b}$ EE $\xrightarrow{4a}$ EF). In this mechanism, EF is the highest point on the potential energy surface, its energy being 53.4 kcal/mol (II) above that of oxirane (Figure 5). The *direct pathway* (oxirane $\xrightarrow{4a}$ EF) requires 55.9 kcal/mol (Figure 4d).

Conclusions

The first conclusion of this study is that orbital symmetry rules do exert control on ring opening of unsubstituted oxirane molecules. The allowed conrotatory process is favored by 10.9 kcal/mol compared to the disrotatory one (Figure 5). This difference in activation energies is lower than that generally expected for pure hydrocarbons (for example, an experimental estimate for ring opening of cyclobutene is 15 kcal/mol).³⁵ Nevertheless, the electronegativity of the central oxygen atom, leading to a rather high diradical character in carbonyl ylide, is not sufficient to make the two concerted ring opening modes competitive in the unsubstituted molecule. This result could have been guessed from previous calculations on cyclopropane ring opening: despite the diradical nature of the ring opened form (trimethylene diradical), the conrotatory motion is still favored by 2 kcal/mol.³² Furthermore, the highest point on the disrotatory reaction path has not the properties of a transition-state structure: this point at which the electronic destabilization is maximum is located at the top of a hill, and only very strong geometrical constraints, such as those occurring in cyclic carbonyl ylides,³⁶⁻³⁸ seem able to force the system to use this pathway.

A second conclusion concerns the cis-trans isomerization reaction occurring through CC bond breaking. As pointed out under Nonsynchronous Ring Opening, the best way to perform this reaction involves the intermediate formation of the planar carbonyl ylide (Figure 5). Therefore, the reaction begins by conrotatory ring opening of oxirane, followed by a rotational isomerization in the carbonyl ylide which finally recloses in a conrotatory manner to the isomer (Figure 5). On this reaction path, the highest point is the transition state for rotational isomerization in carbonyl ylide, i.e., the orthogonal EF structure. It is remarkable that it is precisely this mechanism, avoiding the direct formation of EF

structure (Figure 4d), which has been most often used in the reaction schemes proposed for cis-trans isomerization of oxirane molecules.⁶⁻¹¹

Third, the conrotatory transition-state energy is 5.8 kcal/mol lower than the transition state for rotational isomerization in carbonyl ylide (Figure 5). Therefore, in the absence of steric constraints in carbonyl ylide, cycloaddition following the ring opening is predicted to be stereospecific, in agreement with experimental results (1g and 1h, for example). Concerning the loss of stereospecificity observed in sterically hindered species, our study shows that, among the two mechanisms recalled in the introduction, (i) rapid cis-trans isomerization following the formation of carbonyl ylide or (ii) direct disrotatory reaction path, the former is less energetic. Indeed, the transition state for rotational isomerization in carbonyl ylide is 5.8 kcal/mol above that for conrotatory ring opening instead of 10.9 kcal/mol for the highest point on the disrotatory path (Figure 5). This difference of 5.1 kcal/mol between the two processes leads us to believe that it should be easier, using suitable substituents, to make the rotational isomerization rather than the disrotatory process competitive with the conrotatory ring opening mechanism. If this conclusion is correct, the crucial factor governing the stereochemical course of the reaction would be the energy difference between conrotatory ring opening (Figure 4b) of oxirane to carbonyl ylide and rotational isomerization in carbonyl ylide (Figure 4a). Positive values would mean that the carbonyl ylide formed by conrotatory ring opening has not enough rotational energy to isomerize before being trapped by a dipolarophile (no loss of stereoselectivity). On the contrary, negative values would make possible a rapid rotational isomerization in carbonyl ylide, leading to a loss of stereoselectivity.¹⁰ According to our calculations, this difference is 5.8 kcal/mol in the unsubstituted molecule. This value is close to that found experimentally for *trans*-2-phenyl-3-*p*-tolylloxirane (4.3 kcal/mol),⁶ a compound which leads to a carbonyl ylide free of steric constraints, two hydrogen atoms being in the endo positions (1d \rightarrow 2d). This difference decreases to 3 kcal/mol¹¹ for α -cyano-*trans*-stilbene oxide 1h, a compound which exhibits no loss of stereoselectivity. When bulky groups appear in endo positions in the carbonyl ylide generated by a conrotatory ring opening of oxirane, negative values are obtained for this energy difference: -0.9 kcal/mol⁶ for *cis*-2-phenyl-3-*p*-tolylloxirane 1e and -2 kcal/mol¹¹ for α -cyano-*cis*-stilbene oxide 1i, a compound which precisely shows a lack of stereoselectivity in cycloaddition reactions. Therefore, in so far as our results on the unsubstituted parent molecule can be used as a guide for the discussion of substituted cases, the loss of stereoselectivity in the ring opening of oxirane is likely to originate from a rapid rotational isomerization in carbonyl ylide intermediate.³⁹

Finally, in the light of preceding results, the computational approach used in this study may be commented on briefly. The optimizations have been made by using a minimal basis set followed by a limited CI calculation (method I). Then the reaction paths have been recomputed by using an extended basis set and large CI calculations (method II). First, note that the improvement of the calculations lowers the computed absolute energies by ~ 2 au (~ 1250 kcal/mol). Nevertheless the potential energy curves associated with the various mechanisms are qualitatively similar in both kinds of calculations, the energy barriers differing by only a few kilocalories per mole (see Results). Two factors can explain the qualitative agreement between both

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(39) **Note Added in Proof:** However, one must note that our calculations do not definitely exclude a loss of stereoselectivity arising from the nonsynchronous ring opening (4d) whose activation energy is only 2.5 kcal/mol above that of the rotational isomerization mechanism. As pointed out by a referee, this pathway can be seen as a "forbidden" pathway since it can eventually lead to the product formally implied to be the result of disrotation. The transition state for mechanism 4d would then appear as a more stable Jahn-Teller distorted form of the symmetrical transition state involved in the synchronous disrotatory motion. Therefore, if the words "forbidden reaction path" also apply to the nonsynchronous pathway 4d, it is much more difficult to decide from our calculations whether the partial loss of stereoselectivity arises from rotational isomerization in carbonyl ylide or from the "forbidden" nonsynchronous pathway.

type of calculations: (i) extension of the basis set does not lead to drastic changes in the optimized geometrical parameters characterizing the most important structures. For instance, if EE and EF structures are reoptimized by 4-31G calculations followed by 3×3 CI, their energies are only 1.3 (EE) and 1.9 (EF) kcal/mol lower than those gotten by using the geometries optimized with method I (STO-3G + 3×3 CI); (ii) whatever the point on the potential energy surface, the most important configurations in the correlated wave function are by far those involved

in the limited 3×3 CI. Both these factors lead us to think that the use of the rather crude method I as a first approach is a reasonable compromise between the need for qualitatively correct results and the cost of calculations. From a quantitative point of view, calculations of type II, which include a large part of correlation effect, are necessary to be confident in the numerical values used to discuss the reaction mechanisms.

Registry No. Oxirane, 75-21-8.

A New Route to Functionalized *trans*-Hydrindenones

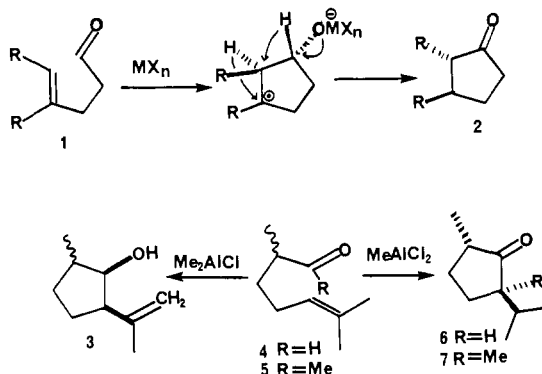
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Abstract: MeAlCl₂-initiated cyclization of dienone **12** provides the functionalized *trans*-fused hydrindenone **15** in 50% yield. Ketone **15**, which is now readily available in three steps from hydrocinnamic acid via this novel cyclopentanone synthesis, has been converted to **27** and **30**, thus completing a formal total synthesis of 11-oxo steroids.

Introduction

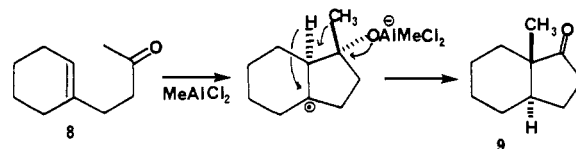
One of the challenging problems in steroid synthesis is the construction of the *trans*-fused CD ring systems present in most steroids.¹ An examination of Lewis-acid-initiated cyclization of unsaturated carbonyl compounds has led us to a new solution to this problem. Treatment of aldehyde **1** (R = H or alkyl) with a Lewis acid leads to the cyclopentanone **2**.^{2,3} We have examined the Lewis-acid-initiated cyclization of **4**.⁴ Depending on the strength and amount of Lewis acid, either ene adduct **3**⁵ or cyclopentanone **6** can be obtained selectively. MeAlCl₂ (1–2 equiv) converts **4** to **6** at –78 °C and converts the ketone **5** to cyclopentanone **7** in 60% yield at 0 °C. We therefore chose to investigate the cyclization of methyl ketones related to aldehyde **1** as a route to *trans*-fused hydrindanones.



Treatment of the methyl ketone **8**⁶ with 2 equiv of MeAlCl₂ in CH₂Cl₂ at 25 °C for 24 h leads to the *trans*-fused hydrindenone **9** in moderate yield. The stereochemistry of **9** is established by

the absorption of the methyl group in the NMR spectrum (δ 0.88) which is 0.15 ppm upfield from that of the *cis* isomer.⁷

The harsh conditions required for this cyclization appeared likely to limit its generality and preclude its application to more highly functionalized systems. We were therefore gratified by the successful cyclization of the unstable dienone **12** to the hydrindenone **15** which is reported here.



Results and Discussion

Birch reduction (Na/NH₃, CH₃OH, –78 to –33 °C)⁸ of hydrocinnamic acid (**10**) gives a 60:40 mixture of **11** and **10**. This mixture of acids cannot be separated chromatographically. Iodolactonization (I₂, NaHCO₃) of this mixture converts **11** to lactone **13** which is separated from **10** by base extraction of **10**.⁸ Treatment of lactone **13** with Zn in acetic acid regenerates **11** (40% overall yield) which is converted to methyl ketone **12** (82% yield) by treatment with 2 equiv of methyl lithium.⁹ Separation of **10** and **11** is not necessary, since, on treatment with methyl lithium, **10** is converted to 4-phenyl-2-butanone which can be separated easily from **15** after cyclization.

The cyclization of **12** to **15** proved to be very sensitive to reaction conditions. Treatment of **12** (0.3 M in CH₂Cl₂ containing 2.7% BHT) with 1.1 equiv of 1.40 M MeAlCl₂ in heptane in a sealed tube under N₂ for 2 h at 90 °C gives **15** in 47–53% yield.¹⁰ Small amounts of 4-phenyl-2-butanone (~10%) and polymer account for the remainder of the material. The survival of the sensitive dihydrobenzene moiety indicates the versatility of the cyclopentanone synthesis. Although other Lewis acids were not in-

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(10) The amount of Lewis acid used is not critical. However use of <1 equiv leads to complex mixtures since uncomplexed ketone can abstract a proton from the zwitterionic intermediate. Similarly, use of >2 equiv leads to complex mixtures. MeAlCl₂ disproportionates in the presence of a deficiency of base. The active species may be the AlCl₃-ketone complex with Me₂AlCl acting as proton scavenger. The presence of traces of water or oxygen has a very deleterious effect on the reaction.