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Cyano, Amino, and Trifluoromethyl Substituent Effects on the Claisen Rearrangement

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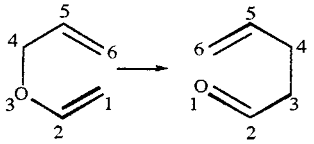
Ab initio quantum mechanical methods with the B3LYP/6-31G* method were used to model the reactants, transition states, and products of Claisen rearrangements of allyl vinyl ethers substituted at all positions with CN, NH_2 or CF_3 groups. The calculations predict that 1-CN, 1-CF_3-cis, 5-NH_2, 6-CN, and 6-CF_3 substituents increase the activation barriers, in agreement with experimental results on substituent effects by CN, CF_3, and the related 5-OCH_3 example. All other substituents lower activation energies. A Marcus theory type analysis was applied to separate the intrinsic and thermodynamic contributions to the activation energies.

Introduction

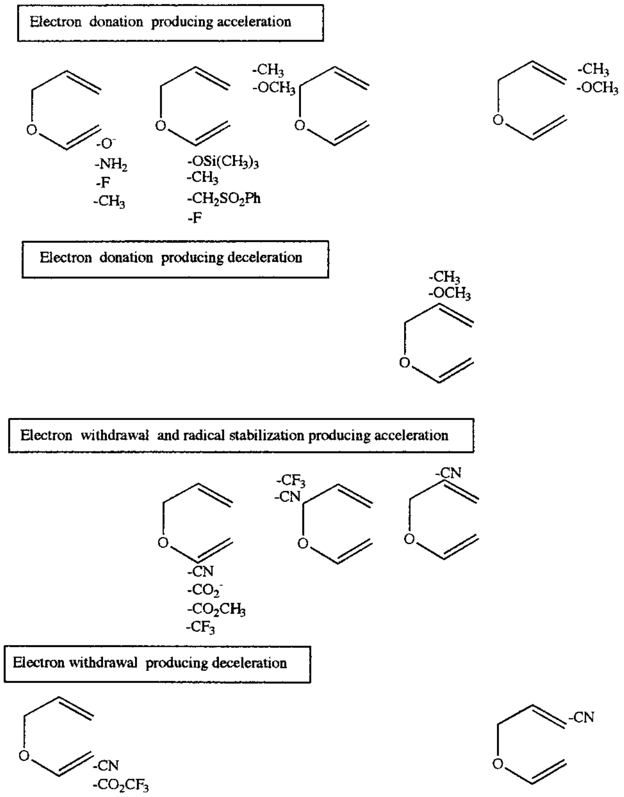
We have extended our previous study[1,2] of the effects of substituents on the rates of Claisen rearrangements. The ultimate goal of this computational work is to assess the intrinsic effect of prototypical conjugating electron-withdrawing, electron-donating, and inductive electron-withdrawing groups represented here by CN, NH_2, and CF_3, on the activation barrier for this rearrangement reaction. All the possible monosubstituted CN, NH_2, and CF_3 allyl vinyl ethers as well as their transition states and products have been modeled and are discussed here.



Experimental Substituent Effect

The Arrhenius parameters for isomerization of allyl vinyl ether (AVE) have been reported in the gas phase[3a] and in solution,[3b] and a large number of substituent effects have been measured for this reaction.[4−10] A qualitative survey of the experimental rate behavior of various monosubstituted allyl vinyl ethers is depicted in Scheme 1.

SCHEME 1: Experimental Rate Behavior of Different Mono-substituted Allyl Vinyl Ethers. The Substituents Are Drawn Next to the Positions of Substituents that Lead to the Effect Noted



The accelerating influence of the electron donating groups such as an oxyanion,[4a] amino,[4b] fluoro,[4c,d] and methyl[4e] at C1 has been experimentally established. Ireland has reported the activation free energy of 2-trimethylsiloxy substituted AVE to be 9 kcal/mol less than that of the parent molecule.[4f] In the gas phase, Frey observed a 1.5 kcal/mol lowering of the activation energy for 2-methyl-AVE as compared to that of the parent.[4g] Denmark and Harmata found that the powerful electron donor, sulfonyl carbanion at position 2 accelerates the Claisen rearrangement.[4h,i] The accelerating effects of donor substituents on the allyl group of the allyl vinyl ether have been thoroughly investigated by Curran et al.[4j] CH_3 and OCH_3 groups at C6 accelerate the rearrangement of 2-OTBS-AVE by 1.2 and 34.3, respectively. The 4- and 6-alkoxy derivatives react 96 and 9.5 times faster than the parent allyl vinyl ether, respectively, whereas 5-methoxy-AVE rearranges 40 times slower than AVE. Wilcox and Babston concluded that for O-allyl-silylketene acetals, the steric bulk at C5 is rate accelerating, whereas electron-donation at C5 is rate retarding.[4k] Recently, Tellier et al.[5a] have shown that the fluorine atom at position 2 for allylfluorovinyl ethers was responsible for a substantial decrease of the rearrangement reaction temperature, thus accelerating the reaction. The unusual reactivity of imidates was rationalized

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on the basis of the stereoelectronic effect of the electron withdrawing phosphonate group at position 4 and an electron donor group (CH_3, Ph, cyc-C_6H_{11}, 2-furanyl, *n*-C_5H_{11}) on C6.[5b]

Accelerations were observed for the cyano group at positions 2, 4, and 5; the rate is 111 times faster for CN at C2, 270 times faster for CN at C4, and 15.6 times faster for CN at C5. The activation free energy for the rearrangement with the CO_2CH_3 group at C2 is 3.0 kcal/mol less than that of AVE itself in dibutyl ether solvent; no reaction was observed for the same group at C6 under the same conditions.[6] The CO_2^- group at C2 slows down the reaction 2.2 times with respect to the CO_2CH_3 group at the same position.[6] The rates of the Claisen rearrangements of the 1-CN and 6-CN derivatives are decelerating and amount to 0.9 and 0.1 times that of the unsubstituted system, respectively.[3b]

To differentiate between inductive electron-withdrawal and a combination of conjugative and inductive electron-withdrawal effects, the C2 and C4 trifluoromethyl allyl vinyl ethers were prepared.[7] CF_3 acts as an inductive electron-withdrawing substituent, but not as a conjugating substituent; CF_3 does not stabilize radicals. The rate of the Claisen rearrangement was found to be accelerated by a factor of 73 by a trifluoromethyl group at C2. At C4, the trifluoromethyl group does not influence the rate, in contrast to the energetic benefit of 3.5 kcal/mol enjoyed by the system when a cyano group is at C4.[7]

Related substituent effects were observed in rearrangements of phenyl propargyl ethers.[8] The asymmetric Claisen rearrangement has been studied,[9] and electron donating groups at position 6 have been found to accelerate the enantioselective Claisen rearrangement of chiral difluorovinyl allyl ethers.[10]

Previous Computational Studies of Substituent Effects. The effects of the CO_2H and CO_2^- groups have been analyzed by Wiest and Houk in connection with a study of the chorismate-prephenate interconversion; a lowering of the activation barrier has been determined for both substituents at C2 and for CO_2^- at C6; whereas CO_2H at C6 is found to increase the activation barrier slightly.[11] Yoo and Houk have reported an accelerating effect for hydroxyl substitution at all positions except for C5. This is in accord with experiment; they developed an analysis of the thermodynamic and intrinsic contributions to rates.[1] Gao et al. have used combined quantum mechanical and statistical mechanical calculations of solvation to show that CN and F at C2, and OCH_3 at C6 accelerate the reaction.[12] These simulations show that the most dramatic substituent effect results from a combination of donor and acceptor substitution; the reaction rate of a 2-CN, 6-OCH_3 substituted AVE is estimated to be 1700 times as fast as that of AVE in water at 25 °C. We previously reported substituent effects for 2 and 6-substituted systems;[2] a decrease in the activation barrier was predicted for the 2-CN, 2-NH_2, and 6-NH_2 derivatives, whereas a large increase in the activation energy was predicted for the 6-CN derivative. The 2-CN and 6-NH_2 groups have been found to decrease the barrier height due to intrinsic contributions. The transition structures for the [3,3] sigmatropic rearrangements of a variety of substituted allyl vinyl sulfides and vinylthioethanimines have been located using ab initio and B3LYP calculations.[13] The results showed that combined donor−acceptor disubstitutions considerably increase the reactivity of the allyl vinyl sulfide. Thus, 2-amino-5-cyano disubstitution lowers the enthalpy of activation by 6.6 kcal/mol and increases the exothermicity of the rearrangement by 13.0 kcal/mol at the MP4SDTQ/6-31G*//B3LYP/6-31G* level.

Although the effects of miscellaneous substituents on the rates of the Claisen rearrangement have been analyzed experimentally and theoretically,[14] there has not been a systematic study of the effect of both donor and acceptor substituent at every position on allyl vinyl ether. Here, we provide such a study and analyze whether predicted rate effects are due to intrinsic or thermodynamic factors.

Computational Methods

Quantum mechanical calculations were carried out using Gaussian 94.[15] Among the activation barriers calculated for the Claisen rearrangement with various methods, the MP4 and B3LYP/6-31G* calculations have shown the best agreement with experimental values.[16−18] B3LYP/6-31G* has also been used to model transition structures for a variety of allyl vinyl sulfides and vinylthioethanimines[13] as well as hetero-Cope type rearrangement reactions.[18] We have used the B3LYP/6-31G* method throughout this study because of its excellent compromise between accuracy and computer time. The conformational search was carried out with respect to rotations about the C2O, OC3, C3C4 bonds for the derivatives of allyl vinyl ether and around the C2C3, C3C4 and C4C5 bonds for the derivatives of pent-4-enal. The stationary points located with PM3 in Spartan 5.0[19] were further fully optimized with B3LYP/6-31G*.

The chairlike transition structure is more stable than the boat, according to experiment and theory.[20] DFT calculations for the Cope rearrangement at all levels find the boat transition structure to be 5−6 kcal/mol higher in energy than the chair structure.[21a] The deuterium and carbon atom kinetic isotope effects with CASSCF/6-31G*[21b] calculations are in excellent agreement with experiment. Recently, the Claisen rearrangement of several allyl fluorovinyl ethers has been shown to occur with the intervention of a chairlike conformation in the transition state.[5] We have adopted the geometry of the chairlike transition structure from our previous work[2] and have introduced substituents at all possible positions. Each stationary point was verified by the calculated harmonic vibrational frequencies as an energy minimum (all real frequencies) or a saddle point (with only one imaginary frequency). Zero point energies have been included in the evaluation of the activation energies and the heats of reactions.

Results and Discussion

Structures. Three different, almost isoenergetic, conformers for allyl vinyl ether, AVE1 (0.0 kcal/mol), AVE2 (+0.03 kcal/mol) and AVE3 (+1.0 kcal/mol), have been located for the parent with B3LYP/6-31G* (Figure 1). In all of them, the dihedral angle about the C2O bond is around 0°, as expected for enol ethers. The only difference between AVE1 and AVE2 lies in the conformation of the allyl ether portion, with the dihedral angle around C4C5 of 0° or ± 120°. The planar conformation of this compound ($<$OC4C5C6 = 0°) is preferred by 0.03 kcal/mol with B3LYP/6-31G*, although AVE2 has been located as global minimum with RHF/6-31G*.[1] As in the case of AVE, three almost isoenergetic conformers were located for pent-4-enal. Note that P1 (+0.0 kcal/mol), P2 (+1.3 kcal/mol), P3 (+1.4 kcal/mol) differ only in the value of the first dihedral angle (Figure 1). The eclipsed conformation of the carbonyl oxygen with C4 in the global minimum can be rationalized by the stabilizing interactions between O and the H's on C3 (2.8 Å). In P2 and P3, only one such interaction (2.6 Å) is possible.

Figure 2 shows the most stable conformers for the reactant (AVE1), the product (P1) and the corresponding transition structure (TS) between them. The bond lengths in the transition state are such that the double bonds of the reactant have been elongated by 4% of their initial values, the C2O3 bond has been

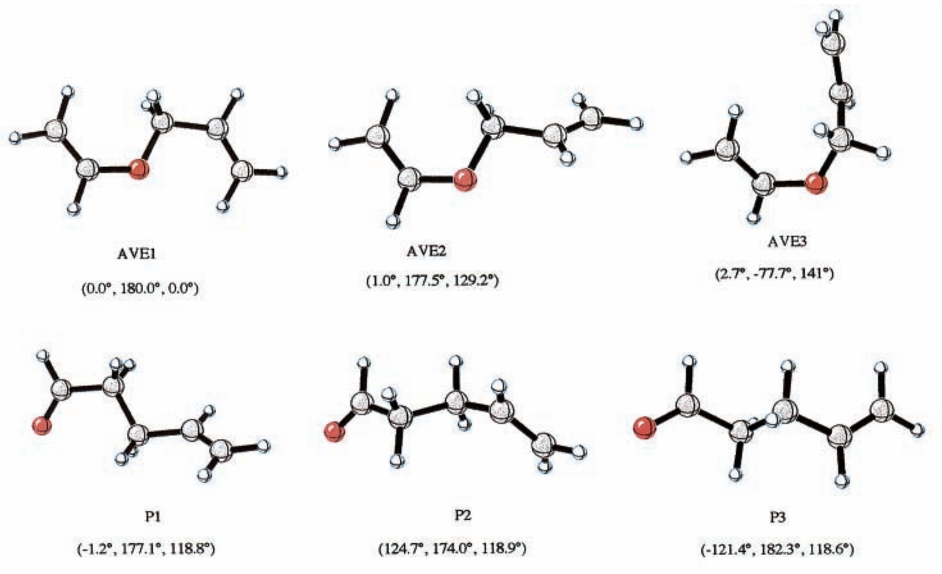


Figure 1. Minimum energy conformers for allyl vinyl ether (AVE1, AVE2, AVE3) and pent-4-enal (P1, P2, P3).

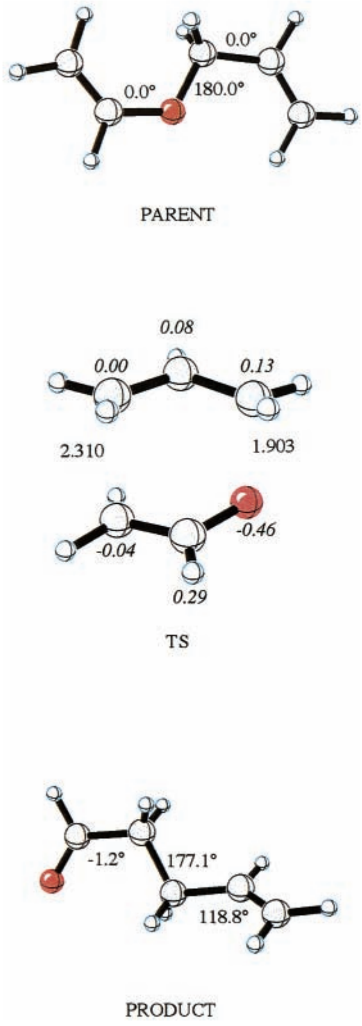


Figure 2. The parent, transition state and product for the rearrangement of allyl vinyl ether.

shortened by 5%, and the breaking O3C4 bond has been elongated by 34% of its initial value. The transition state can be characterized as early and dissociative by these bond length criteria (Table 1).

The optimized structures for the substituted reactants are displayed in Figure 3. Substituents on C1 and C6 may be cis or trans. For all the reactants, except for the 1-X-trans substituted compounds and 4-NH_2, the values of the C1C2OC4 and C2OC4C5 dihedral angles are 0° and 180°, respectively, as in the parent compound, AVE. For the 1-X-trans compounds, the C1C2OC4 angle shifts from 0° to 180°, because the substituent would clash with syn-C4 in the 0° conformer; thus these compounds adopt the C2OC4C5 angle of AVE3. For 6-X-trans substituted compounds, the third dihedral (OC4C5C6) differs from zero; steric repulsions between the substituent and O alter the planarity of the backbone. The bonds at the vicinity of the substituent tend to shorten when the substituent is CF_3 in comparison to the other substituents. This justifies the electron withdrawing character of CF_3 versus CN.

The optimized derivatives of pent-4-enal are shown in Figure 4. They follow the pattern of conformers of the unsubtituted pent-4-enals, namely P1, P2, or P3. The first dihedral angle is around 0° for all the substituted derivatives of pent-4-enal except for P-6-CN and P-6-NH_2, which have angles of 120°. In these compounds, the carbonyl oxygen avoids the syn position with respect to C1C2 because of the bulky substituent on C4. In all of these compounds, the backbone adopts the anti conformation (180°) around the C3C4 bond, and the last dihedral angle is either ±120°.

The optimized transition structures for the parent and substituted allyl vinyl ethers are shown in Figure 5. Bond lengths, changes in bond lengths from reactants, and charges are listed in Table 2. Δ(O3C4), the difference between the breaking bond in the substituted and parent compound correlates roughly with the same difference in the forming bond length, Δ(C1C6). Consideration of these differences reveals the fact that the structures 6-NH_2-cis(trans), 4-NH_2-cis(trans) and 1-NH_2-trans have loose transition states. For substituents at position 5, the forming C1C6 bond in the transition states is shorter in its counterpart in the parent molecule, suggesting early transition states. The relationship between the intrinsic barriers and the geometries of the transition states are addressed in the following sections.

Energetics. The Claisen rearrangement of allyl vinyl ether is exothermic by ~17 kcal/mol.[22,23] A computational study by Yamabe et al. showed that the higher reactivities of allyl vinyl ethers and allyl aryl ethers in comparison with the rearrangements containing heteroatoms N,S, and P other than O are due to thermodynamic factors, especially the greater stability of the

TABLE 1: Bond Lengths of Reactants and Transition Structures for the Claisen Rearrangement of Substituted Allyl Vinyl Ethers at the B3LYP/6-31G* Level

structure	substituent	C1C2	C2O3	O3C4	C4C5	C5C6	C6C1
reactant	H(AVE1)	1.337	1.358	1.420	1.500	1.331	
	H(AVE2)	1.337	1.358	1.430	1.498	1.332	
	H(AVE3)	1.336	1.362	1.430	1.506	1.332	
TS	H	1.383	1.288	1.903	1.402	1.383	2.310
reactant	1-CN-cis	1.348	1.342	1.445	1.501	1.333	
	1-CN-trans	1.352	1.338	1.442	1.497	1.332	
	1-NH_2-cis	1.339	1.384	1.431	1.505	1.333	
	1-NH_2-trans	1.341	1.370	1.414	1.501	1.331	
	1-CF_3-cis	1.338	1.349	1.429	1.505	1.332	
	1-CF_3-trans	1.341	1.344	1.438	1.497	1.332	
TS	1-CN-cis	1.401	1.267	2.038	1.393	1.382	2.426
	1-CN-trans	1.401	1.271	2.009	1.395	1.382	2.392
	1-NH_2-cis	1.395	1.279	2.088	1.393	1.381	2.590
	1-NH_2-trans	1.396	1.278	1.994	1.396	1.382	2.446
	1-CF_3-cis	1.390	1.278	1.951	1.399	1.382	2.366
	1-CF_3-trans	1.392	1.278	1.974	1.395	1.383	2.328
reactant	2-CN	1.343	1.358	1.425	1.500	1.331	
	2-NH_2	1.345	1.364	1.429	1.499	1.332	
	2-CF_3	1.336	1.354	1.434	1.498	1.332	
TS	2-CN	1.389	1.289	1.904	1.403	1.385	2.270
	2-NH_2	1.387	1.298	1.830	1.412	1.380	2.343
	2-CF_3	1.383	1.285	1.931	1.401	1.383	2.311
reactant	4-CN	1.334	1.369	1.426	1.509	1.331	
	4-NH_2	1.336	1.362	1.450	1.510	1.331	
	4-CF_3	1.330	1.373	1.412	1.507	1.330	
TS	4-CN-cis	1.377	1.293	1.906	1.415	1.372	2.449
	4-CN-trans	1.378	1.295	1.906	1.416	1.374	2.429
	4-NH_2-cis	1.379	1.284	2.072	1.418	1.367	2.539
	4-NH_2-trans	1.377	1.286	2.037	1.414	1.367	2.521
	4-CF_3-cis	1.383	1.293	1.878	1.406	1.384	2.287
	4-CF_3-trans	1.382	1.290	1.890	1.402	1.380	2.324
reactant	5-CN	1.336	1.362	1.422	1.510	1.340	
	5-NH_2	1.336	1.360	1.434	1.506	1.342	
	5-CF_3	1.335	1.368	1.419	1.518	1.331	
TS	5-CN	1.387	1.295	1.779	1.422	1.401	2.164
	5-NH_2	1.382	1.292	1.888	1.409	1.389	2.292
	5-CF_3	1.385	1.292	1.828	1.410	1.390	2.223
reactant	6-CN-cis	1.336	1.362	1.423	1.498	1.342	
	6-CN-trans	1.335	1.362	1.415	1.496	1.340	
	6-NH_2-cis	1.337	1.359	1.447	1.499	1.345	
	6-NH_2-trans	1.338	1.355	1.441	1.490	1.343	
	6-CF_3-cis	1.336	1.359	1.424	1.505	1.334	
	6-CF_3-trans	1.336	1.361	1.417	1.497	1.331	
TS	6-CN-cis	1.389	1.282	1.961	1.394	1.396	2.348
	6-CN-trans	1.388	1.281	1.969	1.393	1.395	2.343
	6-NH_2-cis	1.384	1.276	2.111	1.378	1.402	2.540
	6-NH_2-trans	1.385	1.275	2.105	1.377	1.402	2.462
	6-CF_3-cis	1.386	1.290	1.875	1.405	1.388	2.292
	6-CF_3-trans	1.385	1.286	1.902	1.401	1.385	2.300

TABLE 2: Dipole Moments ($|\mu|$, Debye), Critical Bond Lengths (O3C4, C1C6); Difference in Critical Bond Lengths (Δ(O3C4), Δ(C1C6)) between the Parent and Substituted Transition States; Charge Separation ($\Delta\delta$) and Difference in Charge Separation ($\Delta(\Delta\delta)$) between the Parent and the Substituted Transition States

substituent	$\|\mu\|$	$\Delta\delta$	$\Delta(\Delta\delta)$	O3C4	Δ(O3C4)	C1C6	Δ(C1C6)
H	2.10	0.21	0.0	1.903	0.0	2.310	0.0
1-CN-cis	4.98	0.31	0.10	2.038	0.135	2.426	0.116
1-CN-trans	4.42	0.30	0.09	2.009	0.106	2.392	0.082
1-NH_2-cis	2.61	0.10	−0.11	2.088	0.185	2.590	0.280
1-NH_2-trans	3.47	0.09	−0.12	1.994	0.091	2.446	0.136
1-CF_3-cis	3.33	0.27	0.06	1.951	0.048	2.366	0.056
1-CF_3-trans	2.78	0.27	0.06	1.974	0.071	2.328	0.018
2-CN	4.60	0.28	0.07	1.904	0.001	2.270	−0.040
2-NH_2	1.78	0.20	−0.01	1.830	−0.073	2.343	0.033
2-CF_3	3.10	0.25	0.04	1.931	0.028	2.311	0.001
4-CN-cis	4.04	0.15	−0.06	1.906	0.003	2.449	0.139
4-CN-trans	5.62	0.16	−0.05	1.906	0.003	2.429	0.119
4-NH_2-cis	2.62	0.34	0.13	2.072	0.169	2.539	0.229
4-NH_2-trans	1.82	0.35	0.14	2.037	0.134	2.521	0.211
4-CF_3-cis	2.90	0.17	−0.04	1.878	−0.025	2.287	−0.023
4-CF_3-trans	3.88	0.17	−0.04	1.890	−0.013	2.324	0.014
5-CN	4.99	0.13	−0.08	1.779	−0.124	2.164	−0.146
5-NH_2	3.26	0.22	0.01	1.888	−0.015	2.292	−0.018
5-CF_3	3.17	0.16	−0.05	1.828	−0.075	2.223	−0.087
6-CN-cis	3.09	0.13	−0.08	1.961	0.058	2.348	0.038
6-CN-trans	2.95	0.13	−0.08	1.969	0.066	2.343	0.033
6-NH_2-cis	3.82	0.35	0.14	2.111	0.208	2.540	0.230
6-NH_2-trans	4.35	0.35	0.14	2.105	0.202	2.462	0.152
6-CF_3-cis	1.40	0.17	−0.04	1.875	−0.028	2.292	−0.018
6-CF_3-trans	1.49	0.17	−0.04	1.902	−0.001	2.300	−0.010

C═O in the product.[16a] The transition state is early and resembles the reactant more than the product in accord with the Hammond postulate.[24] The reaction of 2-NH_2-AVE is calculated to be exothermic by −33 kcal/mol, 15 kcal/mol more than the parent. The findings for the amino substituent are similar to the calculated results of Yoo and Houk on hydroxy substituents. The rearrangement of the 2-OH compound is the most exothermic reaction in the hydroxy series.[1] Amide or ester resonance in the products causes these extreme exothermicities. By contrast, both cis and trans 1-CN-AVE's are stabilized by conjugation of the cyano group with the electron-rich enol ether; the reactions of these compounds are less exothermic than the reaction of the unsubstituted case. The same is true for 1-CF_3-AVE which is stabilized by inductive and negative hyperconjugation involving the CF_3 group. The trans isomer of 1-CF_3-AVE is stabilized further by long-range interactions between H on C-2 and fluorine of CF_3. The reactions of both cis and trans 4-CN-AVE are more exothermic than that of the parent by 9 kcal/mol, because the product is a resonance-stabilized acrylonitrile. The exothermicities of the rearrangements of the 6-CN and 6-NH_2 allyl vinyl ethers are smaller than in the case of the parent because of the conjugation in the acrylonitrile and the enamine reactants.[25]

The amount of charge transferred, $\Delta\delta$, from the allyl to the oxyallyl moieties in the transition state is 0.21 for the parent compound. The allyl moiety bears a partial positive charge, and the oxyallyl moiety bears a partial negative charge. The charge separation is increased by CN and CF_3 on the oxyallyl part, or by NH_2 on the allyl part.

As described in earlier publications,[1,2] in order to understand how substituents influence the reaction energetics, we have used Marcus theory[26] (equation 1) as applied by Murdoch[27] to pericyclic reactions. This permits a separation of intrinsic and thermodynamic contributions to the activation energy

$$\Delta E^{\ddagger} = \Delta E_0^{\ddagger} + \frac{1}{2}\,\Delta E_{\rm rxn} + (\Delta E_{\rm rxn})^2/16(\Delta E_0^{\ddagger}) \qquad (1)$$

$\Delta E^{\ddagger}$ is the activation barrier for the reaction. $\Delta E_{\rm rxn}$ is the energy of reaction, and the intrinsic barrier, $\Delta E_0^{\ddagger}$, is that of a hypothetical thermoneutral process. The "thermodynamic contribution" is an estimate of how much the change in activation energy caused by the substituent is due to an alteration of the heat of reaction, based on the assumption that potential surface behaves as two overlapping parabolas representing reactant and product energies. For the energies involved here, the equation is essentially equivalent to the assumption that 1/2 of the change in $\Delta E_{\rm rxn}$ appears as a change in $\Delta E^{\ddagger}$.

The energy components for the parent and substituted allyl vinyl ethers deduced this way from the B3LYP/6-31G* calculations are listed in Table 3. The activation energy is lowered by all the substituents except for 1-CN, 1-CF_3 (trans), 5-NH_2, 6-CN, and 6-CF_3. Scheme 1 shows that the 1-CN, 5-OCH_3, and 6-CN substituted allyl vinyl ethers are all experimentally found to

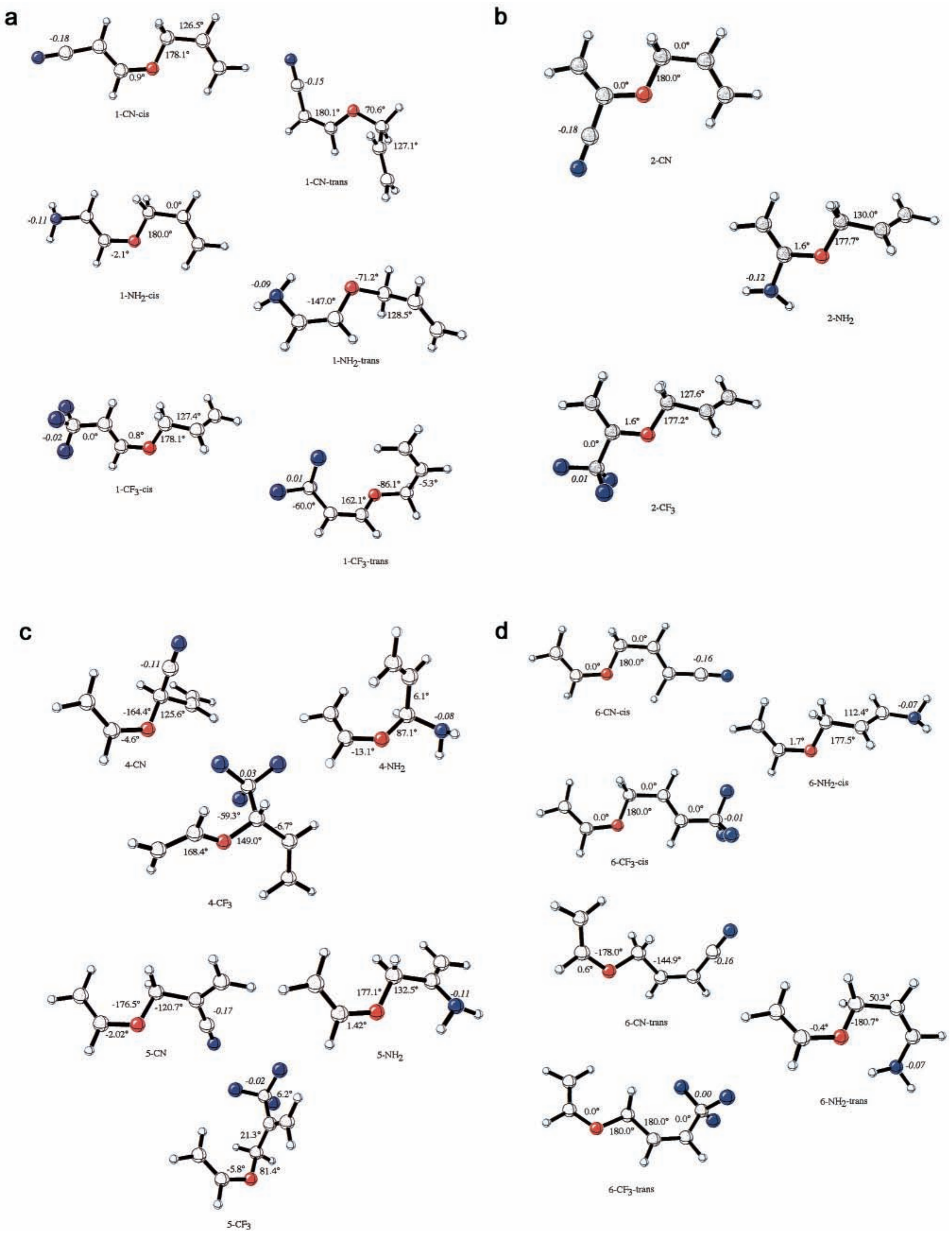


Figure 3. Minimum energy conformers for substituted allyl vinyl ethers.

lower the rate of reaction, in accordance with this prediction. The relative intrinsic and thermodynamic contributions to the activation barriers of the substituents are shown in Scheme 2.

The transition structures have polarized diradical character, because C−O bond breaking exceeds C−C bond making in the transition state. Thus, an electron donor at the C4 and C6 positions can stabilize the partially positive charge on the allyl portion of the molecule in the transition state. As expected, the NH_2 group at C4 and C6 has lowered the intrinsic activation barriers. The conjugating (and radical-stabilizing) CN group behaves in a similar fashion but is less effective. CF_3 at C4 or C6 does not alter the kinetic behavior of AVE. In the oxyallyl

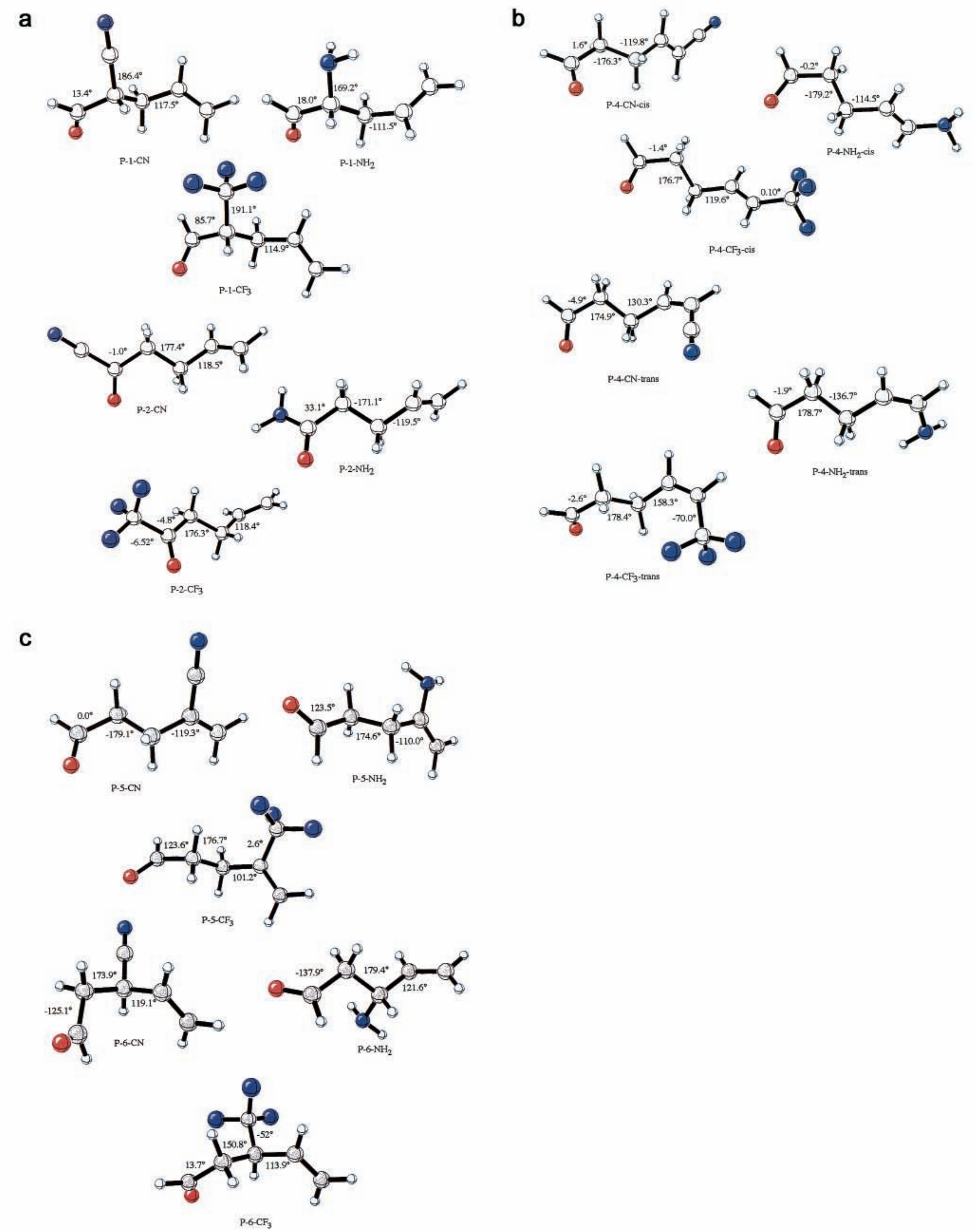


Figure 4. Minimum energy conformers for substituted pent-4-enal.

portion, CN stabilizes the transition state at position 1 by induction and resonance, whereas an NH_2 at the same position stabilizes the transition state inductively. Notice that CF_3 at C1 lowers the kinetic barrier only slightly. The intrinsic behavior of CN and CF_3 (stabilization) and NH_2 (destabilization) at position 5 cannot be explained adequately with this simple polarized diradical model, because this position is located on the partially positive allyl cation moiety in the transition state. However, these effects are likely to arise from the variable radical contribution at this center. Calculations on cyano and vinyl-substituted 1,5-hexadienes reported by Borden et al. provided computational evidence for a chameleonic transition

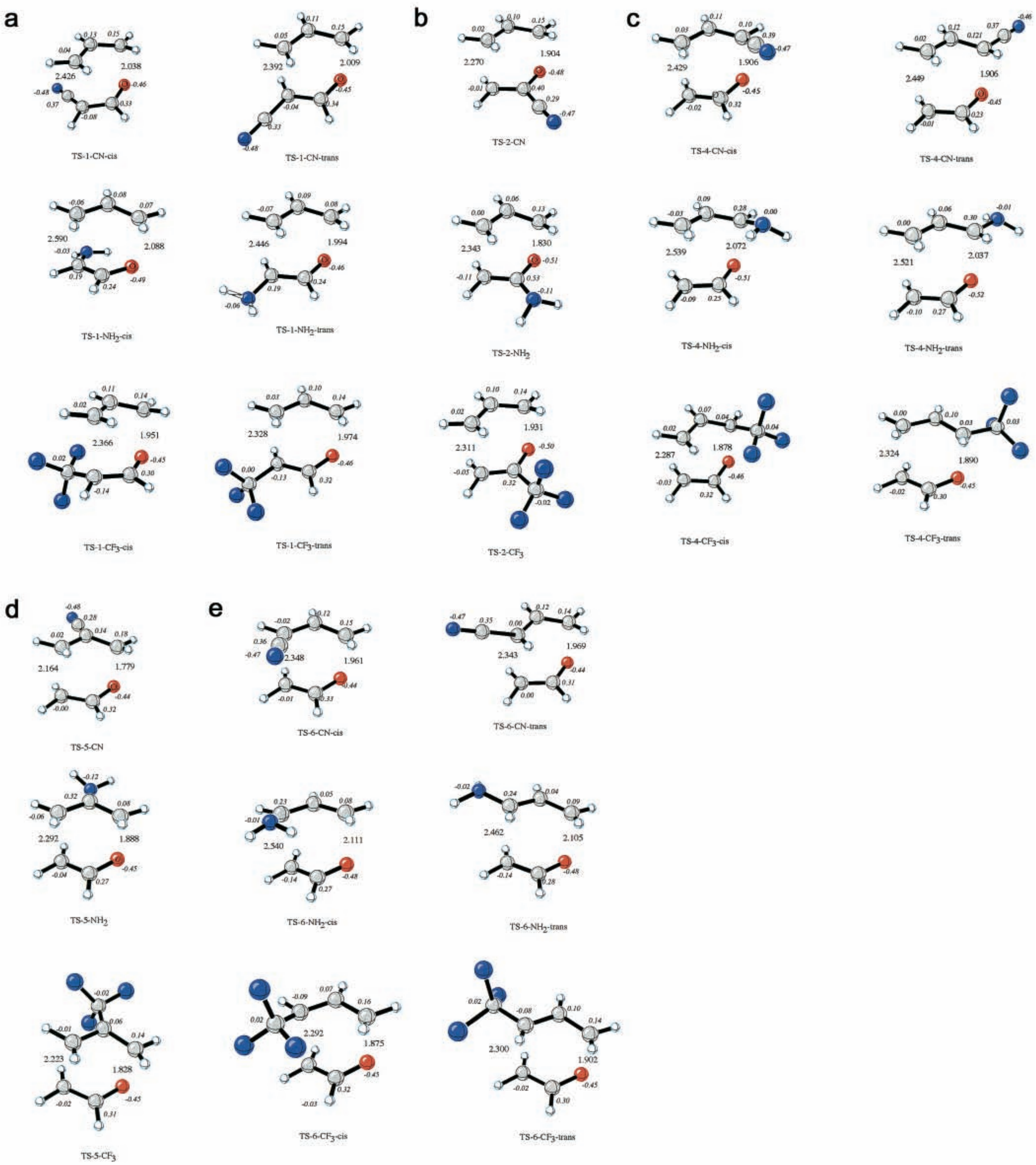


Figure 5. Transition structures for the rearrangement of substituted allyl vinyl ethers.

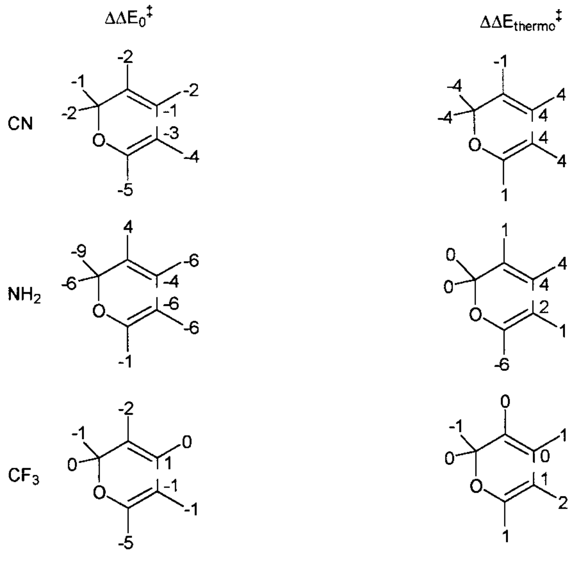
state.[28] Their findings are consistent with a transition structure in which the relative importance of the cyclohexane-1,4-diyl and bis-allyl radical resonance contributors can be altered by substituents, depending on the carbons to which the substituents are attached. Substituents at C2 and C5 have a much larger stabilizing effect than substituents at the four other carbons of 1,5-hexadiene. Alterations in the barrier heights by the cyano group at C1(+2.3), C2(−5.2) and C3(−3.9) for the Cope rearrangement mimic qualitatively our findings on the Claisen rearrangement at C6(+2.1), C5(−2.4) and C4(−5.3), respectively. The lowering of the barrier by CN at C2 for the Cope rearrangement is almost twice as large as for the Claisen. The 1,4-diyl resonance contributor in the transition state for allyl vinyl ether is not as large as in the case of 1,5-hexadiene because the transition state is earlier and more dissociative.

The breaking and forming bond lengths in the transition structure complement the discussion on the chamelonic transition state. These critical distances are shorter for the CF$_3$ group at C1,C4, and C6 indicating an early transition for this electron withdrawing group at these positions. On the other hand, the transition state is early for the electron donor NH$_2$ group and the electron stabilizing CN group at C2 and C5, respectively.

TABLE 3: Activation Energies, $\Delta E^{\ddagger}$, Reaction Energies, ΔE_{rxn}, Intrinsic Barriers, $\Delta E_0^{\ddagger}$, Relative Thermodynamic Contributions to the Activation Barrier (kcal/mol), $\Delta\Delta E^{\ddagger}$(thermo), for the Reaction of Parent and Substituted Allyl Vinyl Ethers. Values Relative to the Parent Are Given In Parentheses

compound	$\Delta E^{\ddagger}$	ΔE_{rxn}	$\Delta E_0^{\ddagger}$	$\Delta\Delta E^{\ddagger}_{thermo}$
parent	27.7	−18.3	36.3	(0)
1-CN-cis	28.3 (0.6)	−10.2 (8.1)	33.2(−3.1)	(3.7)
1-CN-trans	27.8 (0.1)	−9.1 (9.2)	32.2 (−4.1)	(4.2)
1-NH_2-cis	23.2 (−4.5)	−15.0 (3.3)	30.2 (−6.1)	(1.6)
1-NH_2-trans	22.2 (−5.5)	−17.4 (0.9)	30.2 (−6.0)	(0.5)
1-CF_3-cis	27.6 (−0.1)	−16.0 (2.3)	35.2 (−1.2)	(1.1)
1-CF_3-trans	28.8 (1.1)	−13.0 (5.3)	35.0 (−1.3)	(2.4)
2-CN	23.9 (−3.8)	−16.5 (1.8)	31.6(−4.7)	(0.9)
2-NH_2	21.0 (−6.7)	−33.3 (−15.0)	*35.7* (−0.6)	(−6.1)
2-CF_3	23.9 (−3.8)	−17.0 (1.3)	31.8 (−4.5)	(0.7)
4-CN-cis	22.5 (−5.2)	−26.8 (−8.5)	34.6 (−1.7)	(−3.5)
4-CN-trans	22.9 (−4.8)	−27.1 (−8.8)	35.2 (−1.1)	(−3.7)
4-NH_2-cis	21.9 (−5.8)	−18.3 (0.0)	30.3 (−5.9)	(0.1)
4-NH_2-trans	19.1 (−8.6)	−19.0 (−0.7)	27.8 (−8.5)	(−0.1)
4-CF_3-cis	27.3 (−0.4)	−17.7 (0.6)	35.6 (−0.7)	(0.3)
4-CF_3-trans	26.5 (−1.2)	−21.6 (−3.3)	36.5 (0.2)	(−1.4)
5-CN	25.3 (−2.4)	−20.1 (−1.8)	34.6 (−1.7)	(−0.7)
5-NH_2	32.2 (4.5)	−17.1 (1.2)	40.3 (4.0)	(0.5)
5-CF_3	25.9 (−1.8)	−17.7 (0.6)	34.2 (−2.1)	(0.3)
6-CN-cis	29.8 (2.1)	−10.7 (7.7)	34.9 (−1.4)	(3.5)
6-CN-trans	30.3 (2.6)	−9.5 (8.8)	34.8 (−1.5)	(4.1)
6-NH_2-cis	27.5 (−0.2)	−10.2 (8.1)	32.4 (−3.9)	(3.7)
6-NH_2-trans	25.4 (−2.3)	−10.2 (8.1)	30.3 (−6.0)	(3.7)
6-CF_3-cis	28.9 (1.2)	−18.0 (0.3)	37.4 (1.1)	(0.1)
6-CF_3-trans	29.3 (1.6)	−15.7 (2.3)	36.7 (0.4)	(1.2)

SCHEME 2: Intrinsic ($\Delta\Delta E_0^{\ddagger}$) and Thermodynamic ($\Delta\Delta E_{thermo}^{\ddagger}$) Contributions to the Activation Barrier (kcal/mol) for CN, NH_2, and CF_3 Substituents



The thermodynamic contributions to the activation barriers are often significant. CN and NH_2 at position 6 stabilize the reactant by resonance and increase the barrier height. A 2-NH_2 substituent accelerates the reaction mainly by product stabilization. Similarly, a 4-NH_2 substituent stabilizes the product by an anomeric effect, and the activation barrier for NH_2 at C4 is lowered.

The activation barriers for cis and trans isomers are different in some cases because of special interactions. The cis isomer of 6-NH_2-AVE is more stable than the trans isomer because of long-range stabilizing interactions between the ether oxygen and the hydrogen of the amino group as seen in Figure 3. This interaction is lost in the transition structure, and the barrier for the reaction of *cis*-6-NH_2-AVE is higher than that for the trans isomer. The 4-NH_2-AVE can give two products (Figure 4). The amine group is quasi-axial in TS-4-NH_2-cis and quasi-equatorial in TS-4-NH_2-trans; the former transition structure is destabilized.

Recent experimental results by Wood et al.[29] on the transformation of α-diazoketones with allylic alcohols to furnish intermediate enols which undergo Claisen rearrangement to α-hydroxyketones confirm our calculated results. The CH_3 group at C4 accelerates the reaction, whereas at C5 it slows down the reaction. The rate retarding behavior of trifluoroacetate as compared to CH_3 at C1 has also been emphasized by the authors. Calculated results for NH_2 at C1, C4, C5 and for CN at C1 reproduce exactly the same trend (Table 3).

Conclusion

B3LYP/6-31G* calculations parallel substituent effects found in experimental studies. The effects of a donor and acceptor substituents on the rate have been rationalized with the difference in geometrical parameters and charge separation between the parent and the substituted allyl vinyl ethers. A quantitative evaluation of the intrinsic barriers is accomplished with Marcus theory.

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