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Polarized π-Frontier Molecular Orbitals. A Method for Predicting Diastereofacial Selectivities

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Abstract: A method of breaking the symmetry of the π-orbitals of nonsymmetrical molecules with respect to their nodal planes is described. The new (polarized) orbitals have different coefficients associated with each face of each π-center. These coefficients can be used for predictive purposes in a manner analogous to simple frontier orbital theory. In order to break the symmetry of the atomic p-functions, each new p-orbital is constructed from a normal p-function and two additional Gaussian s-type functions, one superimposed over each lobe of the p-function. This new method (polarized π-frontier orbitals, PPFMO) is illustrated using the placement of different functional groups (H, CH_1, OH, CN) on a carbon adjacent to π-systems containing from one to four carbon π-centers (methyl, ethylene, allyl, butadiene). The effects of the various substituents adjacent to carbon π-systems cannot be categorized completely in terms of electron-withdrawing and electron-donating effects. The effects are greatest on the smaller π-systems and on the nearest carbon centers. The substituent effects on the polarization of the FMO's are shown to be quite different from those on their energies. FMO theory is adapted to include both effects. A comparison of PPFMO theory with earlier proposals made by Anh and Cieplak is discussed in terms of the predicted effects on FMO's.

The question of how electronic effects influence diastereofacial selectivity in organic chemistry has been the subject of much recent debate. Several earlier proposals have been made by Felkin,[1] Anh,[2] and Cieplak.[1] Felkin and Anh have suggested that interaction between the bonding orbital being formed and the antibonding orbitals of adjacent bonds might be the controlling factor, while Cieplak places more importance in the interaction between the antibonding orbital of the incipient bond and the bonding orbitals of the adjacent bonds. Much of the discussion of these models has centered on the selectivity of the reduction of cyclohexanone. These suggestions have been recently reviewed by le Noble, who also adds some interesting analyses.[4] These proposals have been criticized by Frenking,[5] Paddon-Row,[6] and Houk,[7,8] who have performed molecular orbital calculations on the reaction paths for carbonyl addition and other related reactions.

We have been interested in the understanding of selectivities similar to those for the reactions of free radicals and cycloadditions. While there has been much debate on the electronic causes of diastereofacial selectivity of the Diels–Alder reaction in the literature, most of the discussion involving free radicals is based upon steric arguments.[9]

Frontier molecular orbital theory (FMO)[10,11] has often been used with some success in predicting reactivity and regioselectivity of various reactions. Although we[12,11] have suggested that this methodology be used with some caution, as it considers only the reagents (not the transition state), the simplicity of its application argues for its use in appropriate situations. We have suggested that FMO theory might be best applied (a) when the reaction is likely to have an early transition state, (b) when the perturbational effect being considered is large, and (c) when there is conformational correlation between the reagents and products.[12,11]

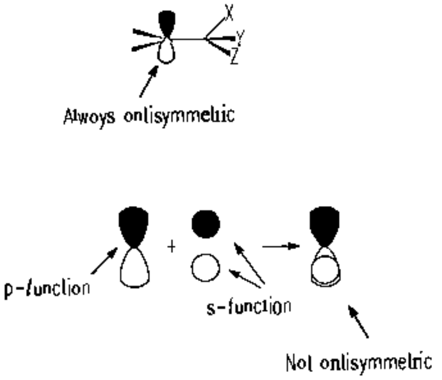

Figure 1. Schematic representation of the combination of a p-orbital with two s-functions.

In this paper, we shall present an extension of FMO theory which is a new method of predicting π-diastereofacial selectivity. The theory is illustrated by application to acyclic π-systems containing from one to four π-centers. We critically evaluate the treatment of carbonyl reductions by this method in comparison with other theoretical and experimental results in another paper.[14]

Description of the Methodology. The atomic p-orbitals used in simple molecular orbital treatments are rigorously antisymmetric. Thus, one cannot use the coefficients of these orbitals to predict diastereofacial selectivity in a manner similar to that employed in FMO theory to predict regioselectivity. In this paper

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(1) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* 1968, 2201.

(2) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* 1977, *1*, 62.

(3) Cieplak, A. S. *J. Am. Chem. Soc.* 1981, *103*, 4540.

(4) Li, H.; le Noble, W. J. *Recl. Trav. Chim. Pays-Bas* 1992, 111, 199.

(5) Frenking, G.; Koehler, K. F.; Reetz, M. T. *Angew. Chem.* 1991, *10J*, 1167.

(6) Wong, S. S.; Paddon-Row, M. *J. Chem. Soc., Chem. Commun.* 1990, 456.

17) Wu, Y.-D.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* 1987, *109*, 5560.

(8) Wu, Y. D.; Tucker, J. A.; Houk, K. N. *J. Am. Chem. Soc.* 1991, *113*, 5018.

(91 Giese, B. *Angew. Chem., Int. Ed. Engl.* 1989, *28*, 969.

(10) Fukui, K. *Acc. Chem. Res.* 1971, *4*, 57.

(11) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: New York, 1976.

(12) Dannenberg, J. J.; Franck, R. W. *J. Org. Chem.* 1985, *50*, 2635.

(13) Kaila, N.; Franck, R. W.; Dannenberg, J. J. *J. Org. Chem.* 1989, *54*, 4206.

(14) Huang, X. L.; Dannenberg, J. J. *J. Am. Chem. Soc.*, submitted.

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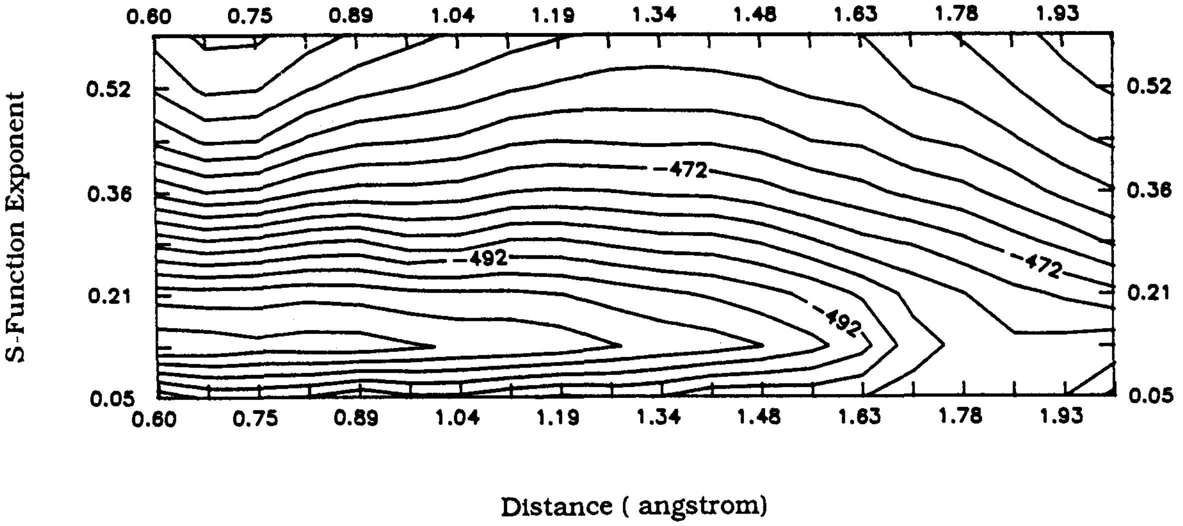

Figure 2. Contour plot of the total energy (hartrees) as a function of the distance from the carbons and the orbital exponents of the s-functions for allyl alcohol.

we describe a simple construct that allows us to desymmetrize the p-orbitals for the purpose of applying a simple FMO interpretation. We call this new application polarized π-frontier molecular orbital (PPFMO) theory.

The basic construct is the superposition of two new basis functions, one upon each lobe of an atomic p-function (Figure 1). The p-orbital would then be constructed from a linear combination of these three functions. The original antisymmetry of the p-function will be tempered by the two additional functions, which can differ in magnitude. The difference in magnitude between these functions will indicate the extent to which the π-orbital is polarized at each particular atomic site. This polarization, in turn, can be used to predict the diastereofacial selectivity according to approximations normally associated with FMO theory. The polarization, p, is given by eq 1, where c_+ and

$$p = c_+\chi_+ + c_-\chi_- \qquad (1)$$

c_- are the coefficients on the s-type basis functions χ_+ and χ_-, respectively. The +/− notations correspond to the sign of the lobe of the p-orbital on which the new basis function is superimposed. A positive value of p signifies polarization in the direction of the positive lobe of the p-orbital.

Two initial observations will be extremely important: (a) only small basis sets should be used and (b) the geometries must be optimized using another method. The use of only small basis sets is dictated first by the need to keep the method as simple as possible. However, one must also consider the fact that the larger the basis set, the less influence the added Gaussians will have. At the extreme of the Hartree–Fock limit, the addition of the two new Gaussians would have no effect whatever. The need to use another method for optimization comes from the destruction of the spherical symmetry of the atoms whose basis sets have been augmented by the added Gaussians. Optimization with such a basis set would not give reasonable geometries.

For the reasons indicated above, we have chosen to use the simple STO-3G basis set for our studies. The p-orbitals whose polarizations we are trying to determine are augmented by two s-type Gaussians. The exponents of these Gaussians and their distances from the nuclei have been determined by analysis of the effects of these parameters upon the results in the manner indicated below. A model compound (allyl alcohol) was first optimized using the AM1[15] semiempirical method. Single-point STO-3G calculations were performed using the Gaussian88 and Gaussian90 computer programs.[16] The s-functions were positioned along the axis of the π p-orbitals at varying distances from the carbon nuclei. The exponents of the Gaussians were also varied. A plot of the total energy as functions of both the distance from the carbon nucleus and the exponent of the Gaussian is displayed in Figure 2. For this figure, allyl alcohol in the conformation having the C–OH bond coplanar with the π-system was used. Gaussian s-functions were superimposed over each of the two p-orbitals involved in the double bond. The total energy generally increases with the distance from the nucleus (see Figure 2). This result is likely due to the difficulty that small Gaussian basis sets have with adequately describing the cusp in the electron density at the nucleus. At virtually all distances from the nucleus, the minimum energy occurred with an orbital exponent of slightly greater than 0.1. Rather than simply using the energetically optimal distance and exponents, we tempered the relationships depicted in Figure 2 by our desire to maximize the magnitude of desymmetrization. We chose a distance from the nucleus of 1.3 Å, as Figure 2 shows the energy to be a shallow function of this distance until about 1.3 Å, above which it increases more rapidly. Similarly, we chose a value for the exponent of 0.1 (slightly less than the energy optimum) to keep the effect localized.

In the cases considered in this paper, the π-systems were kept rigorously planar. In general, this may not be the case. This problem is addressed in another paper on carbonyl reductions.[14]

A complete integration into the mathematical (second-order perturbational) treatment that is used in FMO theory (eq 2) is presented in eq 3, where ΔE_{face} is the difference in the perturbational energies for the two faces of the π-system. The summation over i is for all of the two-center interactions between the HOMO and LUMO (e.g. one for carbonyl reductions or reactions of free radicals, but two for cycloadditions such as the Diels–Alder reaction). Equation 3 is illustrated for a polarized LUMO interacting with a nonpolarized HOMO. For a polarized

$$\Delta E_{\text{interaction}} \propto \frac{\sum_i c_i^{\text{HOMO}} c_i^{\text{LUMO}}}{E^{\text{LUMO}} - E^{\text{HOMO}}} \qquad (2)$$

$$\Delta E_{\text{face}} \propto \frac{\sum_i p_i^{\text{LUMO}} c_i^{\text{HOMO}}}{E^{\text{LUMO}} - E^{\text{HOMO}}} \qquad (3)$$

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(15) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(16) Gaussian, Inc., Pittsburgh, PA.

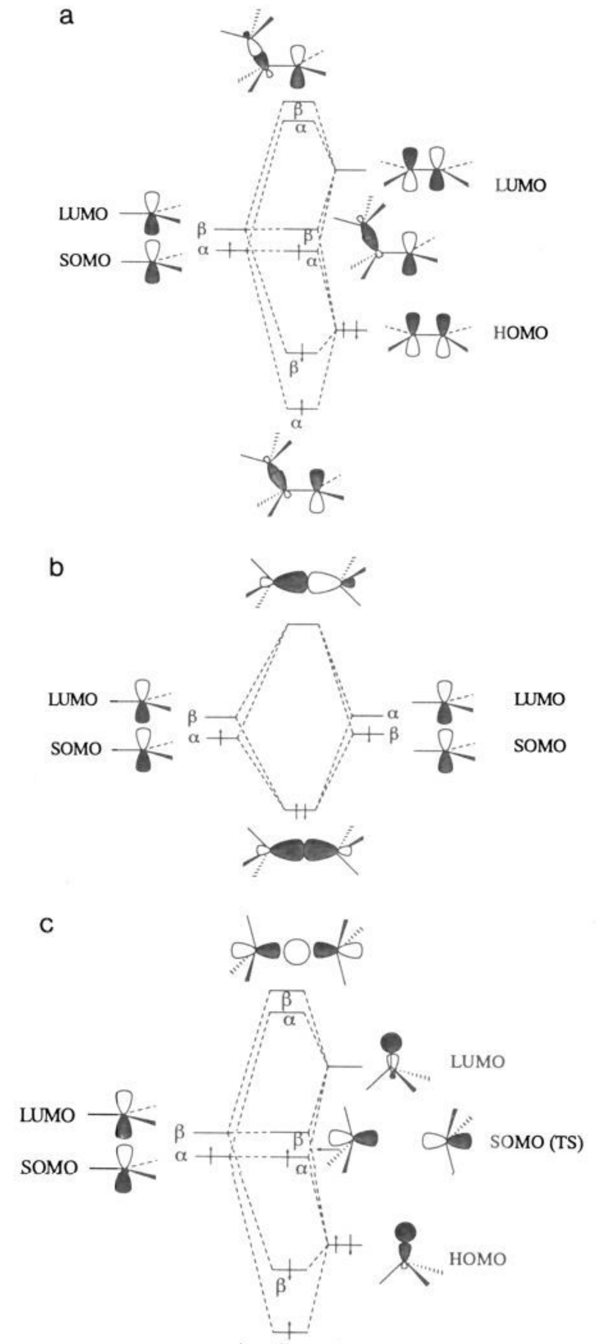

Figure 3. FMO diagrams of the interactions for (a) radical addition to an alkene; (b) radical–radical combination; and (c) atom (H) transfer. Note that the center orbitals represent the product for diagrams a and b but the transition state for diagram c; note also that, for atom transfer of a larger atom (e.g., halogen), the central orbital in the transition state would be a p-orbital so the symmetries of the bonding and antibonding combinations would be reversed.

HOMO interacting with a nonpolarized LUMO, p^{HOMO} and c^{LUMO} should be used in the summation.

For calculations on free radicals, UHF/STO-3G calculations have been performed. In these cases the singly occupied molecular orbital (SOMO), which is the HOMO of the α spin orbitals, is used in place of the HOMO. The LUMO is the lowest unoccupied β spin orbital. FMO theory for free radical reactions can sometimes be more complicated than for closed shells. Thus, a radical addition to an alkene would involve both the interaction between the radical SOMO and the alkene LUMO, and that of the radical LUMO with the alkene HOMO. The product of the addition would, itself, be a radical. Since the SOMO's of alkyl radicals (for example, ethyl radical) generally have a node between the α and β carbons,[17] one might expect that the interaction of the SOMO of the original radical with the LUMO of the alkene leads to the SOMO of the new radical (see Figure 3a). For radical–radical couplings (Figure 3b) and disproportionation reactions, each radical contributes one electron. In these cases, the SOMO of one will interact with the LUMO of the other and vice versa. For atom-transfer (abstraction) reactions, one might expect the interaction of the radical SOMO with the highest energy filled orbital involving the C–H bond to be dominant (Figure 3c).

Results

α-Substituted Free Radicals. The results for substituted methyl radicals are collected in Table I. Each of the calculations involves a methyl radical substituted with a substituent that breaks the symmetry of the p-orbital's nodel plane. In the first three cases, the α carbon has two C–H bonds. The third bond, which is kept parallel with the axes of the π p-orbital, was varied. From examination of Table I, one sees that although the polarization of both the SOMO and LUMO of the radical change with substituent, the changes are not what one would necessarily expect from simple arguments based upon the electron-donating or -withdrawing abilities of the substituents relative to hydrogen. With the exception of the SOMO of the methyl-substituted case (where there is no polarization), all substituents lead to polarizations that predict attack at the face opposite to the substituent in both the SOMO and LUMO. A methyl substituent, generally thought to be electron-donating, has little effect upon the orbital energies of either the SOMO or LUMO (compared to H). However, the slight polarization of the SOMO disappears, while the more moderate polarization of the LUMO is significantly increased. Hydroxyl, the weaker of the two electron-withdrawing groups (as evidenced by the lowering of the orbital energies) somewhat increases the polarization of the SOMO, while enormously increasing the polarization of the LUMO (from 0.044 to 0.222, compared to H). The cyano group, which is the most electron-withdrawing substituent, provides the greatest (yet, still moderate) increase in polarity of the SOMO but the smallest increase in polarization of the LUMO (again, compared to H).

Two-Center π-Systems (Substituted Alkenes). As can be seen from Table II, the effect upon the proximal center of the two π-centers is much greater than that upon the other. As in the case of the one-π-center system, the general tendency of the polarization in both the HOMO and LUMO favors attack anti to the substituent. The only exception is the slight polarization toward syn attack predicted for the HOMO of the methyl-substituted case. In the one-π-centered case, methyl reduced the polarization of the SOMO to zero. Here, it reverses the polarization of the HOMO for the proximal center. The two electron-withdrawing groups both increase the polarization of the HOMO for the proximal center, but the order is reversed with hydroxyl having a larger effect than cyano. For the LUMO, only cyano increases the polarization of the proximal π-center, while both methyl and hydroxyl decrease it. The polarizations of the distal center are lower by almost an order of magnitude. For the HOMO, they are opposite to that of the proximal center in each case, but only that for hydroxyl is reasonably large. For the LUMO, the distal polarization is opposite to that at the proximal center for all cases except cyano. Two of the substituents (methyl and cyano) have reasonably large polarizations.

Three-Center Systems (Substituted Allyl Radicals). Once again, the proximal carbon is polarized to suggest attack anti from the substituent in all cases except for the HOMO in the

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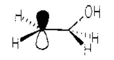
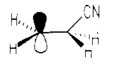
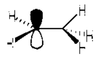
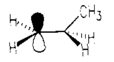
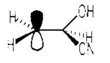
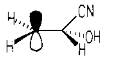
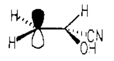
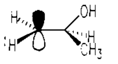
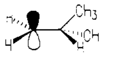
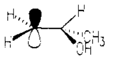
[17] Dannenberg, J. J.; Baer, B. *J. Am. Chem. Soc.* **1987**, *109*, 292.

Table I

compound	ΔH(AM1) (kcal/mol)	E^{SOMO} (hartree)	E^{LUMO} (hartree)	polarization, p		coefficient, p_π		coefficient, χ^a	
				p^{SOMO}	p^{LUMO}	c^{SOMO}	c^{LUMO}	c^{SOMO}	c^{LUMO}
	−26.11	−0.339	0.132	−37	−222	802	409	220 −257	509 −731
	47.69	−0.352	0.120	−56	−100	806	418	181 −237	586 −686
	15.49	−0.313	0.146	−17	−44	798	396	225 −242	641 −685
	10.91	−0.312	0.147	0	−112	786	397	250 −250	613 −725
	9.57	−0.365	0.112	−29	−202	792	420	197 −226	498 −700
	8.37	−0.355	0.122	−20	−9	797	431	197 −217	616 −625
	7.92	−0.354	0.120	−28	45	767	419	208 −236	664 −619
	−30.25	−0.335	0.138	−42	−218	794	414	213 −255	512 −730
	−31.80	−0.318	0.149	18	2	743	417	248 −230	660 −658
	−31.89	−0.318	0.142	−50	40	725	404	205 −255	676 −636

[a] The coefficients of χ are listed for χ_+ (upper value) and χ_- (lower value) for each entry.

methyl-substituted case (Table III). The polarizations are generally smaller than in the previous cases. Both electron-withdrawing groups increase the polarization in both the SOMO and LUMO, while methyl reverses the polarization of the SOMO but increases that of the LUMO. The effects upon the distal center are small without a clear trend.

Four-Center Systems (Substituted Butadienes). These systems were considered in their s-cis conformations, as these are significant for cycloadditions (Table IV). Here the effects are further attenuated, particularly for the HOMO. Nevertheless, for the proximal center the general trend is the same as that for the two-center systems. The effect on the LUMO is significant in all cases with the electron-withdrawing groups augmenting and the methyl group diminishing the polarization, in contrast to the two-center cases.

Chiral Substituents. When the substituent is made chiral by substituting the α carbon with one hydrogen and two different other substituents, the effect of the polarization upon acyclic systems will depend upon the polarization of each rotamer and the relative energies of the FMO's as well as those of the rotamers. As can be seen from Tables I–IV, the most polarized rotamer may not have the optimal FMO energy or be the most stable. Thus, the complexity of the combined effects makes simple predictions of the face selectivities in these systems difficult.

Discussion

The results suggest that the perturbational effect upon the polarization of the π-system may be very different from the effect upon the orbital energies. If this be the case, then some perturbational arguments made previously, which are based solely upon considerations involving orbital energies, may not be valid. For example, comparison of the results for substituted ethyl radicals shows that when a methyl substituent is exchanged for an electron-withdrawing group, such as cyano, the LUMO is lowered in energy, as one would expect. Thus one would expect the incipient bonding orbital formed from this LUMO with another orbital to be stabilized when the cyano group is anti. However, the polarization of the LUMO is greater for the hydroxyl-substituted radical. If one compares the effects of cyano vs hydroxyl, the orbital energy difference is smaller, and the polarization difference larger.

Perhaps the best means of evaluating the effects of substituents on face selectivities would be to combine the polarization effects with the energetic perturbation of the relevant FMO's. For the case of a reagent whose polarized LUMO is to react with a generalized nonpolarized HOMO, the relative reactivities could be calculated from eq 3, where c_j^{HOMO} and E^{HOMO} are both constants. This leads to eq 4, where the constant, K, is the product

$$\Delta E_{\mathrm{face}} = K\sum_i \frac{p_i}{E^{\mathrm{LUMO}} - E^{\mathrm{HOMO}}} \tag{4}$$

of all constants. In this equation, E^{HOMO} is also a constant. Since $E^{\mathrm{HOMO}} \leq 0$ (as all bonding orbitals must be more stable than a free electron), it can be replaced by another constant, $-k$, where $k \leq 0$ (eq 5).

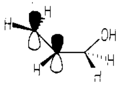
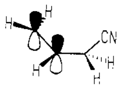
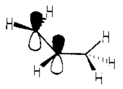
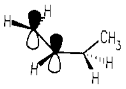
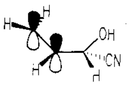
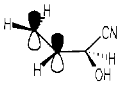
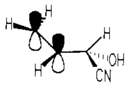
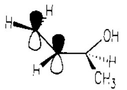
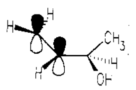
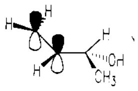
$$\Delta E_{\mathrm{face}} = K\sum_i \frac{p_i}{E^{\mathrm{LUMO}} + k} \tag{5}$$

In many MO calculations, the LUMO is calculated to have a positive energy (although this need not always be true). The highest energy the HOMO of a nucleophile can have is 0. If we assume that $E^{\mathrm{HOMO}} = -k = 0$, then eq 4 becomes eq 6. The difference in the relative reactivities of competing reactions will decrease as the HOMO becomes more stable.

$$\Delta E_{\mathrm{face}} = K\sum_i \frac{p_i}{E^{\mathrm{LUMO}}} \tag{6}$$

For cases where a polarized HOMO interacts with a generalized LUMO (as in electrophilic attack), a similar development yields

Table II

compound	ΔH_f (AM1) (kcal/mol)	E^{HOMO} (hartree)	E^{LUMO} (hartree)	polarization, p				coefficient				coefficient, χ[a]			
				HOMO		LUMO, p_π		HOMO		LUMO		HOMO		LUMO	
				p_β	p_α	p_β	p_α	c_β	c_α	c_β	c_α	c_β	c_α	c_β	c_α
	−38.01	−0.348	0.155	32	−98	−9	−104	477	451	384	447	162 −130	4 −102	795 −804	703 −807
	38.56	−0.365	0.151	7	−42	−21	−132	520	507	376	480	151 −144	60 −102	789 −810	667 −799
	6.84	−0.339	0.173	6	−12	7	−113	533	487	353	484	170 −164	73 −85	822 −815	706 −819
	0.82	−0.339	0.171	−4	11	26	−90	529	481	357	474	156 −160	100 −89	836 −810	731 −821
	−1.84	−0.371	0.139	50	−76	12	−179	494	476	394	458	174 −124	19 −95	783 −771	629 −808
	−2.77	−0.370	0.147	1	−23	14	17	515	506	386	493	143 −142	68 −91	795 −781	712 −695
	−2.91	−0.372	0.143	6	−14	5	−170	501	486	385	465	140 −134	88 −102	794 −789	656 −826
	−43.18	−0.343	0.164	34	−112	−1	−51	471	442	378	476	167 −133	−18 −94	808 −809	715 −766
	−43.62	−0.345	0.167	9	1	71	51	514	470	364	495	144 −135	110 −109	852 −781	769 −718
	−43.81	−0.342	0.165	22	−24	13	−116	450	411	373	469	139 −117	71 −95	823 −810	714 −830

[a] The coefficients of χ are listed for χ_+ (upper value) and χ_- (lower value) for each entry.

eqs 7 and 8. Here, k represents the energy of the LUMO of the

$$\Delta E_{\text{face}} = K \frac{\sum_i p_i}{k = E^{\text{HOMO}}} \qquad (7)$$

$$\Delta E_{\text{face}} = -K \sum_i \frac{p_i}{E^{\text{HOMO}}} \qquad (8)$$

electrophile, which is arbitrarily set to zero in eq 8. Analogous to the case for nucleophilic attack, the differences in relative reactivities decrease as the LUMO of the nucleophile increases in energy.

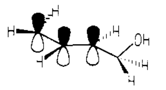
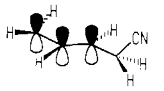
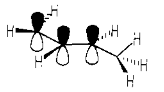
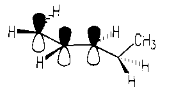
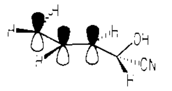
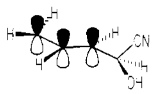
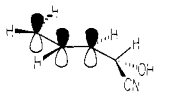
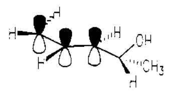
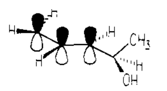
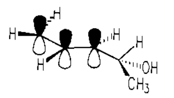
The largest polarizations calculated were for the one-center π-systems, the simple free radicals. For each of the individual substituents considered, the polarizations of the p-orbital were all in the anti direction for both SOMO and LUMO (except for the SOMO of the n-propyl radical, where $p = 0$). In a recent review of the stereoselectivities of intermolecular free-radical reactions, Giese has shown that addition reactions and atom-transfer reactions generally occur anti to substituents on the β carbon of the radical.[9] He attributed this observation to the differences in the steric requirements in the transition states for the reactions of interest. While the steric effect is certainly important (probably dominant in most if not all cases discussed by Giese), one should note that the electronic effects also favor attack in the same direction.

The diastereofacial selectivities of Diels–Alder reactions have been of interest for some time. We have previously indicated that these selectivities can be complicated mixtures of steric and electronic factors that are difficult to understand in simple terms.[13] The present results do little to alter that assessment. The optimized transition states previously reported all have their shorter (i.e. stronger) bonds at the unsubstituted end of the diene. While the polarizations of the HOMO's are generally small for the dienes, they virtually vanish for the unsubstituted end.

Comparison of our results with the suggestions of Cieplak and Anh are informative. Replacing a hydrogen with a methyl group that is parallel to the axis of the π-system has a negligible effect upon the energies of the HOMO's and LUMO's of all the π-systems studied (about 0.001 eV). On the other hand, the effect on the polarization varies significantly (from a change of 0.078 to 0.004) with the methyl-substituted case more polarized in the cases with one π-center and less polarized in the other three cases for the adjacent p-orbital in the LUMO. As both the Anh and Cieplak models take only the orbital stabilization into account, they necessarily miss the polarization effect.

The Cieplak model, originally proposed to explain the nucleophilic attack on cyclohexanone, assumes that the principal stabilization can be approximated by equation 9.[3] In this equation, SE is the stabilization energy; S, the overlap; σ_i, the doubly occupied orbital vicinal to the incipient bond; and $\sigma^*_{\ddagger}$, the

Table III

compound	ΔH_f (AM1) (kcal/mol)	E^{SOMO} (hartree)	E^{LUMO} (hartree)	polarization, p				coefficient				coefficient, χ			
				SOMO		LUMO, p_π		SOMO		LUMO[a]		SOMO		LUMO	
				p_γ	p_α	p_γ	p_α	c_γ	c_α	c_γ	c_α	c_γ	c_α	c_γ	c_α
	−22.52	−0.3056	0.1213	−3	−32	4	−141	572	626	387	391	207 −210	167 −199	538 −534	290 −431
	51.41	−0.3181	0.1116	−4	−38	−2	−69	573	634	401	400	202 −206	149 −187	533 −535	332 −401
	19.18	−0.2926	0.1283	2	−21	12	−52	542	644	408	374	211 −209	161 −182	602 −590	289 −341
	13.40	−0.2920	0.1273	0	12	6	−48	540	635	403	378	207 −207	198 −186	580 −574	319 −367
	13.32	−0.3180	0.1107	−9	−131	3	−284	543	622	392	391	187 −196	071 −202	528 −525	182 −466
	12.86	−0.3146	0.1104	5	57	14	186	516	610	398	399	191 −186	172 −115	540 −526	432 −246
	12.45	−0.3102	0.1095	4	−22	10	−50	516	616	409	387	203 −199	124 −146	583 −573	296 −346
	−27.81	−0.3027	0.1256	−2	−43	−2	−119	571	629	403	388	209 −211	158 −201	567 −569	265 −384
	−28.26	−0.2945	0.1285	2	6	18	−27	541	620	402	389	206 −204	196 −190	574 −556	333 −360
	−28.32	−0.2961	0.1275	3	−27	6	20	545	627	406	377	210 −207	168 −195	598 −592	325 −305

[a] The coefficients of χ are listed for χ_+ (upper value) and χ_- (lower value) for each entry.

$$\mathrm{SE}(\sigma_i,\sigma^*_x) \approx \frac{S^2(\sigma_i,\sigma^*_\ddagger)}{\Delta\epsilon(\sigma_i,\sigma^*_\ddagger)} \tag{9}$$

antibonding orbital of the incipient bond. He emphasizes that the incipient bond is intrinsically electron deficient, very stretched, and very polarized. If one imagines the transition state to be very early (reactant-like), the $\sigma^*_\ddagger$ orbital will be the LUMO of the π-system. Thus, Cieplak's argument is one that focuses on lowering the LUMO under nucleophilic attack in a manner analogous to that of FMO theory.

Anh's model assumes that the antibonding orbital of the σ-bond, σ^*_i, antiperiplanar to the incipient bond will stabilize the latter's bonding orbital, $\sigma_\ddagger$. As $\sigma_\ddagger$ can be thought as coming from the interaction of the LUMO of the π-system with the HOMO of the nucleophile, this analysis also resembles FMO theory. However, when the transition state is very early (as above), $\sigma_\ddagger$ will be the HOMO of the nucleophile, so that this interaction will initially be zero but increase as the reaction proceeds. Thus, this effect should be more important for later transition states, while the Cieplak suggestion should be more important for early transition states.

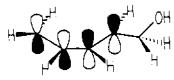
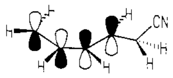
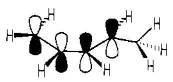
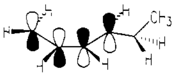
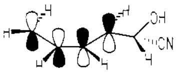
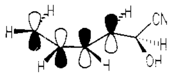
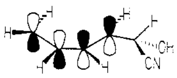
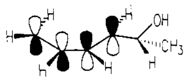
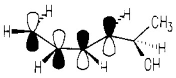
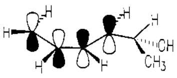
Although the Cieplak and Anh models have been conceived for nucleophilic attacks (reductions of carbonyls), it is instructive to consider other applications. For electrophilic attacks, the above analyses lead to the conclusions that the Ceiplak and Anh models will be reversed in that the former will be important for a later, while the latter for an earlier, transition state. The foregoing should be obvious in that an electrophilic attack is simply a nucleophilic attack where one is considering attack on the nucleophile (rather than the nucleophile as attacking).

For free-radical reactions, one cannot assume that the incipient bonds are particularly polar in character. For both atom transfers and additions to double bonds, the SOMO of the radical should be the major contributor to the incipient bond. This will be true as conservation of spin requires that the SOMO of the product have an electron of the same spin as that of the reagent radical. However, in both cases the radical LUMO's also make significant contributions (see Figure 3a,b). For radical coupling reactions, the SOMO of one radical must interact with the LUMO of the other and vice versa (Figure 3c). Since the two models do not always make the same predictions, it is difficult to determine a clear preference based only on the polarizability.

The advantages of the PPFMO method over both the Anh and Cieplak formulations are (a) an MO calculation on the reagent includes all substituent interactions that affect the reagent rather than focusing on only one and (b) the interactions can be interpreted in terms of the π-polarizations, p, in combination with the effects upon the energies of the HOMO's and LUMO's.

In principle, one can calculate the frontier orbitals and integrate their densities to illustrate how they are polarized in one direction or another (for example see Frenking's calculation of cyclohex-

Table IV

				polarization, p				coefficient				coefficient, χ			
				HOMO		LUMO, p_π		HOMO		LUMO[a]		HOMO		LUMO	
compound	ΔH_f(AM1) (kcal/mol)	E^{HOMO} (hartree)	E^{LUMO} (hartree)	p_δ	p_α	p_δ	p_α	c_δ	c_α	c_δ	c_α	c_δ	c_α	c_δ	c_α
	−21.43	−0.302	0.113	−3	−22	−8	−128	424	439	335	371	119 −122	85 −107	527 −535	377 −505
	52.79	−0.310	0.098	−2	−25	−7	−76	434	440	341	390	122 −124	74 −99	507 −514	411 −487
	20.83	−0.291	0.115	−2	−14	1	−50	430	428	333	387	127 −129	70 −84	544 −543	415 −465
	14.87	−0.290	0.114	1	8	−2	−33	428	424	333	383	130 −129	96 −88	537 −539	439 −472
	14.33	−0.313	0.096	0	−19	−3	−109	435	443	344	380	121 −121	85 −104	501 −504	380 −489
	13.86	−0.308	0.100	−4	−24	−8	−49	431	449	343	384	121 −125	78 −102	510 −518	414 −463
	13.73	−0.310	0.101	−3	−16	10	20	434	437	345	389	122 −125	90 −106	530 −520	443 −423
	−26.73	−0.295	0.113	−2	−29	−10	−105	433	438	341	383	126 −128	80 −109	538 −548	363 −468
	−27.01	−0.290	0.115	−2	4	−1	−11	424	431	337	379	127 −129	102 −98	542 −543	437 −448
	−27.01	−0.292	0.115	−3	−17	3	34	429	423	338	386	125 −128	82 −99	550 −547	444 −410

[a] The coefficients of χ are listed for χ_+ (upper value) and χ_- (lower value) for each entry.

anone[5]). The calculations are generally much more difficult than PPFMO, as a suitable basis set must be used. Graphical depiction is generally necessary. Comparisons between two different molecules are difficult to make. In principle, the difference in the electron densities for the orbitals of the two molecules under study can be obtained. However, since the bond lengths and other structural features will differ, making such a difference surface is not very convenient. Previous discussions of polarizations of π-systems have appeared. Klein et al.[18] as well as Burgess and Liotta[19] have used perturbation arguments to suggest the manner in which the π-orbitals are polarized. Klein's suggestion has been criticized by both Frenking[5] and le Noble.[4] His analysis leads to distortions of the π-orbitals of cyclohexanone that are different than those obtained from PPFMO or ab initio calculations. This subject is discussed in another paper which illustrates the application of PPFMO theory to carbonyl reductions.[14] The treatment by Burgess and Liotta also leads to results different from those obtained by PPFMO. In particular, they expect the same polarizations from any substituent (other than H) on a carbon adjacent to a double bond, while PPFMO theory predicts the polarizations to depend upon the substituent (Table II). Like the Cieplak and Anh models, these perturbation treatments must choose which interaction is dominant and then focus on the appropriate perturbation.

Unlike the methods discussed above, PPFMO theory involves an MO calculation on the reagent. This necessarily includes all interactions between the reactive π-system and all substituents in the molecule. Thus, it is neither important nor necessary to decide which effects will be important and which can be neglected.

Paquette has related the polarization of π-orbitals to deviations from planarity.[20] As PPFMO theory requires no 'orbital tilting,' Paquette's analysis is also somewhat different from what we propose here.

The PPFMO theory is simple and inexpensive to use. Both the AM1 optimizations and STO-3G single-point calculations can be performed in a few minutes on contemporary workstations. It is applicable to electrophilic, nucleophilic, and free-radical reactions. The PPFMO results accord quite well with ab initio calculations on both the polarization of the π-orbitals[5] and favored transition states,[5-8] as well as experimental results for the reduction of carbonyls, as reported elsewhere.[14] The method also successfully predicts the facial selectivities for electrophilic attacks on substituted glycals, also reported elsewhere.[21]

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(18) (a) Klein, J. *Tetrahedron Lett.* **1973**, *29*, 4307. (b) Eisenstein, O.; Klein, J.; Lefour, J. M. *Tetrahedron* **1979**, *35*, 225.

(19) Burgess, E. M.; Liotta, C. L. *J. Org. Chem.* **1981**, *46*, 1703.

(20) Paquette, L. A.; Hsu, L.-Y.; Gallucci, J. C.; Korp, J. D.; Bernal, I.; Kravetz, T. M.; Hathaway, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 5743.

(21) Franck, R. W.; Kaila, N.; Blumenstein, M.; Geer, A.; Huang, X. L.; Dannenberg, J. J. *J. Am. Chem. Soc.*, submitted.