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Characteristics of the Two Frontier Orbital Interactions in the Diels−Alder Cycloaddition

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Two electron-deficient dienes were reacted with a series of twelve electron-poor and electron-rich dienophiles to give, in some cases, the corresponding Diels−Alder adducts. Clear differences in the roles played by the two frontier orbital interactions emerged. It was demonstrated that in the case of normal Diels−Alder cycloadditions, the FMO theory could predict the relative reactivities between dienophiles, while in the case of inverse-electron demand Diels−Alder reactions, it could not. It was shown that the dissymmetry in electron-rich dienophiles increases their reactivities.

The Diels−Alder cycloaddition is arguably one of the most powerful reactions in the arsenal of the synthetic organic chemist.[1] Synthetic plans that incorporate this reaction depend on our ability to effectively predict the relative reactivities of dienes and dienophiles. Studies that can refine or modify the predictive power of existing tools are still very useful. The frontier molecular orbital (FMO) theory as first expressed by Fukui[2] continues to be utilized extensively by synthetic organic chemists to help them predict the reactivity and selectivity of many organic reactions.[3] As pertains to the Diels−Alder reaction, predictions of reactivity and selectivity are normally based on the strength of a single FMO interaction between the diene and dienophile, the so-called "dominant" interaction. The dominant interaction is usually taken to be the one involving the two frontier orbitals having the smallest energy gap between them.[2] As shown in Figure 1, when the $\mathrm{HOMO_{diene}}-\mathrm{LUMO_{dienophile}}$ ($\mathrm{H_{de}}-\mathrm{L_{do}}$) energy gap is least, the reaction is called a normal Diels−Alder cycloaddition (NDAC), while when the $\mathrm{HOMO_{dienophile}}-\mathrm{LUMO_{diene}}$ ($\mathrm{H_{do}}-\mathrm{L_{de}}$) energy gap is smallest, the reaction is dubbed "inverse-electron-demand Diels−Alder cycloaddition" (IEDDAC). This definition presumes that either of these two frontier orbital interactions confer identical stabilization to the transition state for a given energy gap, a presumption that has no solid foundation.[2c,4]

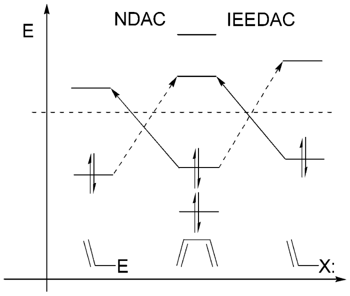

FIGURE 1. Frontier orbitals in the normal and inverse electron-demand Diels−Alder cycloadditions.

While many reactions appear to disobey the FMO rule of reactivity,[5] IEDDA cycloadditions have an inordinate amount of cases in that category. For example, why does the dimerization of acrolein compete effectively with its cycloadditions with electron-rich dienophiles despite typical energy gaps that give the latter 1.5−2.0 eV advantage?[1b] Why do a series of 2-azadienes react with a host of electron-deficient dienophiles including methyl acrylate but none react with ethyl vinyl ether despite FMO energy gaps that favored the latter by 1.5 eV?[6] Why does 2-carbomethoxy-1,3-butadiene **1** dimerize much faster than it reacts with dihydropyran and other electron-rich dienophiles?[7] Inverse electron-demand Diels−Alder cy-

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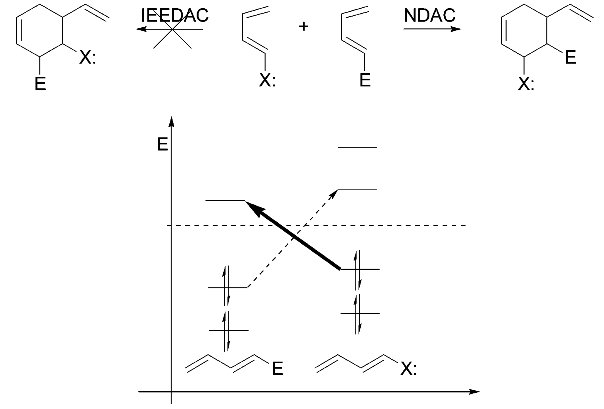

FIGURE 2. The NDAD is always favored over the IEEDAC in cross-Diels–Alder cycloadditions.

cloaddition generally progress under much harsher conditions than normal Diels–Alder cycloadditions,[1b] for comparable $H_{de}-L_{do}$ and $H_{do}-L_{de}$ energy gaps.

We have shown some time ago that the $H_{de}-L_{do}$ interaction exerts a larger influence on the energetics of the Diels–Alder reaction than does the $H_{do}-L_{de}$ interaction.[8] The most convincing experimental support for this hypothesis comes from our observation that NDACs are always favored over IEDDACs in the cross-Diels–Alder cycloaddition between an electron-poor and an electron-rich diene (Figure 2).[8] The fact that the same frontier orbitals are involved in either the NDAC or the IEDDAC removes any possible bias and alleviates the need for calculating orbital energies. This domination of the NDAC over the IEDDAC has nearly no exception, and even strong steric effects did not overcome it.[8] That is to say, the system energetically profits more from a narrower $H_{de}-L_{do}$ than from a narrower $H_{do}-L_{de}$. This is an important observation that emphasizes the preponderance of the $H_{de}-L_{do}$ in influencing the transition structure and thus the reaction rate. Domingo has discussed the [4+2]-cycloaddition of furans with 4-carbomethoxy-6,6-dimethoxy-*o*-quinone.[9] These reactions represent rare examples of a cross-Diels–Alder cycloaddition between two dienes where the IEEDAC is favored over the NDAC. However, the NDAC reaction of furans (i.e. furans acting as the diene) is known to be often reversible.[1c] The reaction was described as proceeding through a stepwise mechanism with the furan acting as a nucleophile, although a NDAC reaction followed by a Cope rearrangement was not ruled out.

Domingo and co-workers have made several contributions on the subject of the mechanism of polar DA reactions.[10] In their analysis,[10a] dienes and dienophiles are ranked according to their calculated global electrophilicity index ω, as described by Parr.[11] It is argued that dienophiles with high ω values should react faster with dienes possessing low values of ω. For example, 1,3-butadiene ($\omega = 1.05$) is expected to react faster with methyl vinyl ketone (MVK, $\omega = 1.65$) than with ethylene ($\omega = 0.73$). In addition, partners with large $\Delta\omega$ are expected to react through a very polar mechanism, which may even be considered as an electrophile–nucleophile reaction rather than a true cycloaddition.[10b] While the difference in ω index is very useful for predicting the relative reactivities of dienes and dienophiles, it is based on FMOs and therefore it has many of the shortcomings of the theory. For example, why does MVK undergo a NDAC with 1,3-butadiene (140 °C, sealed reactor)[12] ($\Delta\omega = 0.60$) but MVK will not undergo an IEDDAC with ethylene even though the $\Delta\omega$ is larger ($\Delta\omega = 0.85$)? MVK undergoes an IEDDAC with methylvinyl ether ($\Delta\omega = 1.23$) under conditions (180 °C, sealed reactor) similar to that needed for the MVK/1,3-butadiene reaction despite a much larger $\Delta\omega$.[13] Here too, IEDDACs pose a problem in the interpretation of the relative reactivities of dienes and dienophiles.

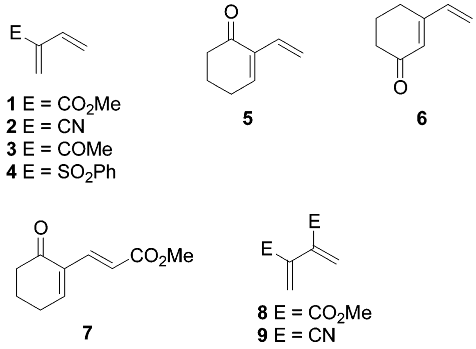

FIGURE 3. Electron-poor dienes **1**–**9**.

Electron-poor dienes such as **1**–**7** (Figure 3) have been known for a long while to react with both electron-deficient and electron-rich dienophiles.[7,14] The ability of these dienes to react with both types of dienophiles offers an opportunity to probe further the role of the two frontier orbital interactions in a single system. To the best of our knowledge, no one has measured which of the electron-deficient or electron-rich dienophiles reacted faster with such dienes. In addition, no one has verified if the FMO theory adequately predicted reactivity trends for each category of dienophiles. Answers to these questions may establish with more precision and detail what influence each of the frontier interactions ($H_{de}-L_{do}$and $H_{do}-L_{de}$) exerts on the rate of Diels–Alder reactions and

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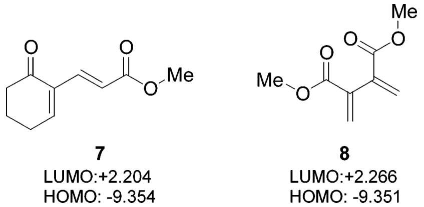

FIGURE 4. Orbital energies (eV) and geometries of dienes **7** and **8**.

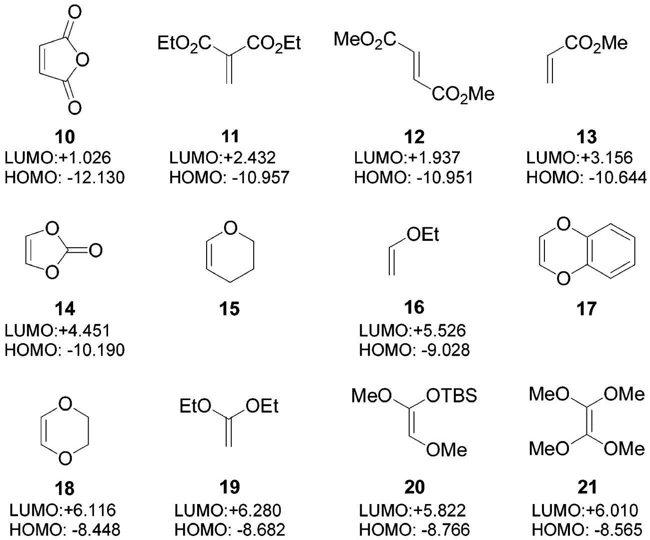

FIGURE 5. Orbital energies (eV) and coefficients of dienophiles **10**−**21**. Trimethoxyethene was used in lieu of diene **20** for the calculations.

thus lead to better predictions of diene and dienophile reactivities. We therefore set out to measure the rates of Diels−Alder cycloadditions of dienes **7**[15] and **8**[16] with several electron-poor and electron-rich dienophiles. We herein report our results, which led to an unexpected observation about the role orbital coefficients may play in the reactivity of dienes and dienophiles. We offer an interesting and novel interpretation of this role.

Results

The minimized geometries and orbital energies for the two dienes are shown in Figure 4.[17] We chose 12 dienophiles, all of which are shown in Figure 5 along with the energies of their frontier orbitals. Tables 1 and 2 list the time of reaction for each dienophile with diene **7** and **8**, respectively.[18] Figures 6 and 7 display their Diels−Alder adducts (in the absence of dienophile, dienes **7** and **8** dimerize to **29** and **37**,[14b] respectively, via a Diels−Alder cycloaddition).

TABLE 1. Kinetic Results of the [4+2]-Cycloaddition of Diene 7 with Dienophiles 10−21

entry	dienophile[a]	adduct	time to completion[b] (h)	yield (%)
1	**10**	**22**	6	100[c]
2	**11**	**23**	4	100[c]
3	**12**	**24**	5.5	100[c]
4	**13**	**25**	14	100[c]
5	**14**			
6	**15**			
7	**16**		(4 equiv) −	
	16	**26**	(neat) 0.5[d]	89[e]
8	**17**			
9	**18**			
10	**19**	**27**	(4 equiv) 1.5	91[e]
			(2 equiv) 2.5	89[e]
11	**20**	**28**	6	100[c]
12	**21**			

[a] 4 equiv of dienophile. [b] Monitored by NMR. [c] Percent conversion by NMR; product decomposes upon chromatography. [d] Microwave oven, EVE as solvent. [e] Isolated yield.

TABLE 2. Kinetic Results of the [4+2]-cycloaddition of Diene 8 with Dienophiles 10−21

entry	dienophile[a]	adduct	time to completion[b] (h)	k_r (mL/mol·s)	yield (%)[c]
1	**10**	**30**	8	0.31	100[d]
2	**11**	**31**	9	0.26	83
3	**12**	**32**	8	0.30	90
4	**13**	**33**	48		30[e]
5	**14**				
6	**15**				
7	**16**				
8	**17**				
9	**18**				
10	**19**	**35**	4	0.77	83
11	**20**	**36**	9	0.24	57
12	**21**				

[a] 2 equiv of dienophile. [b] Monitored by NMR. [c] Isolated yield. [d] Percent conversion by NMR; product decomposes upon chromatography. [e] Gave 30% **33** and 32% **37**.

With respect to both dienes, maleic anhydride (MA; **10**), 1,1-carbethoxyethene (CEE; **11**),[19] and dimethyl fumarate (DMFu; **12**) were of similar reactivities (Tables 1 and 2, entries 1, 2, and 3). Maleic anhydride benefits from a diminished steric encumbrance and a lower LUMO (Figure 5). Methyl acrylate (MAc; **13**) was much less reactive and took 14 h to react with diene **7** (Table 1, entry 4). With diene **8**, it gave approximately a 50−50 mixture of adduct **33** and dimer **37** (Table 2, entry 4). As we moved to more electron-rich dienophiles (e.g. **14**−**18**), the reactivity dropped completely (Tables 1 and 2). Vinylene carbonate (**14**) (entry 5), dihydropyran (**15**) (entry 6), ethyl vinyl ether (EVE; **16**) (entry 7), 2,3-dihydro-1,4-benzodioxane (**17**)[20] (entry 8), and 2,3-dehydro-1,4-dioxane (**18**) (entry 9),[21] were unreactive with dienes **7** and **8** and only the dimer **29** or **37**, respectively, was observed in these reactions. Diene **8** formed dimer **37** even when heated to 150 °C in a sealed tube in neat EVE. However, diene **7** was able to react in neat EVE with microwave heating (Table 1, entry 7) but it was unable to do so with dehydrodioxane **18**. The reactivity

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(18) The dimerization of **7** is slightly faster than that of **8** and a small quantity of dimer **29** often accompanied the desired cycloadducts. This is why we chose to use 4 equiv of dienophiles for this case and we felt that measured reaction rates would be less precise.

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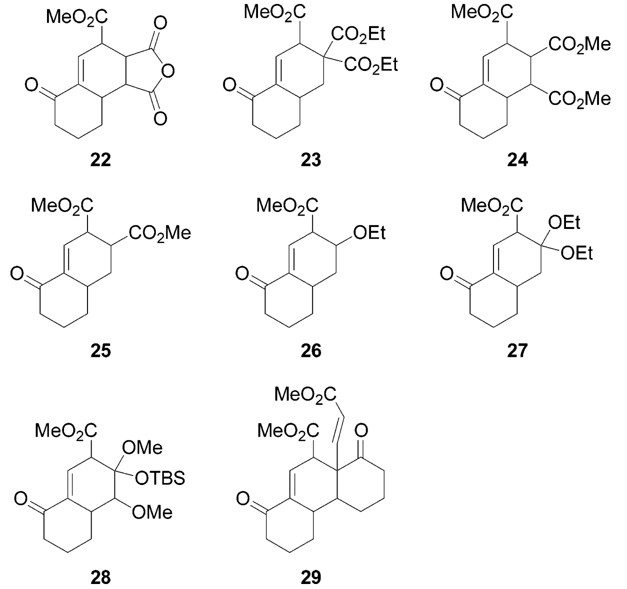

FIGURE 6. Products from the Diels–Alder reaction of diene **7** with dienophiles **10**–**13**, **16**, **19**, and **20**.

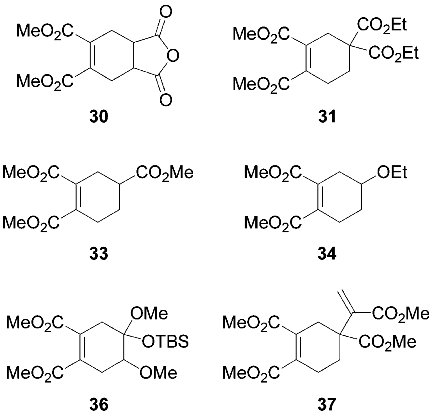

FIGURE 7. Products from the Diels–Alder reaction of diene **8** with dienophiles **10**–**13**, **16**, **19**, and **20**.

TABLE 3. Calculated HOMOs and LUMOs of Diene 8 and Dienophiles 10–14, 16, and 18–21

entry	diene/ dienophile	HOMO	LUMO	$L_{do}-H_{8}$	$L_{8}-H_{do}$	k_{rel}
1	**8**	−9.351	2.266	11.62	11.62	
2	**10**	−12.130	1.026	10.38	14.40	0.31
3	**11**	−10.957	2.432	11.78	13.22	0.26
4	**12**	−10.95	1.937	11.29	13.22	0.30
5	**13**	−10.644	3.156	12.51	12.91	$<$0.26
6	**14**	−10.190	4.451	13.80	12.46	$\ll$0.26
7	**16**	−9.028	5.526	14.88	11.29	$<$0.26
8	**18**	−8.448	6.116	15.47	10.71	$\ll$0.26
9	**19**	−8.682	6.280	15.63	10.95	0.77
10	**20**	−8.767	5.823	15.17	11.03	0.29
11	**21**	−8.565	6.010	15.36	10.83	$\ll$0.26

returned with dienophiles **19** and **20** but not **21**. For instance, 1,1-diethoxyethene (DEE; **19**)[22] was more reactive than MA (**10**) or CEE (**11**) (compare entries 10 with entries 1 and 2 in each table). The trialkoxysubstituted ethene **20**[23] was less reactive than **19** but more reactive than MAc (**13**) (entry 11 vs entries 10 and 4 in each table). Tetramethoxyethylene (**21**)[24] was unreactive (entries 12) and only dimer **29** or **37** was isolated in this case. Dienophiles **11** and **19** are of similar steric hindrance and both are more sterically hindered than the unreactive EVE **16**. We can thus conclude that the electronics is the controlling element in the reactivity of these dienophiles and not steric effects. Steric effects may, however, lower the reactivity of **20** with respect to DEE (**19**).

There are a few differences between the cycloaddition results of dienes **7** and **8**. In the case of **7**, CEE (**11**) was slightly more reactive than MA (**10**) and DMFu (**12**) (entries 1, 2, and 3). In contrast, **11** was slightly less reactive than **10** or **12** with diene **8**. EVE (**16**) was able to react efficiently with diene **7** if a large excess was used with microwave heating (Table 1, entry 7). This was not the case with diene **8**. Finally, **19** was more reactive with **7** than with diene **8** (compare entries 10 in Tables 1 and 2).

Discussion

Table 3 lists the calculated energies of the frontier orbitals for diene **8** and all dienophiles except **15** and **17**. $L_{\mathbf{8}}-H_{do}$ represents the calculated energy gap (eV) between each dienophile with respect to the LUMO of diene **8**. $L_{do}-H_{\mathbf{8}}$ represents the calculated energy gap (eV) between the dienophile's LUMO with respect to the HOMO of diene **8**. The $H_{\mathbf{8}}-L_{\mathbf{8}}$ energy gap is relevant to its dimerization. Note that the energy gaps between the FMOs of the dienophiles and those of diene **7** would be nearly identical since dienes **7** and **8** have nearly identical calculated HOMO and LUMO energies (cf. Figure 4). They were not included in Table 3 for clarity.

One observation is immediately striking: although the $H_{do}-L_{de}$ energy gaps of dienophiles **16** and **18**–**21** are very close in value, their reactivities are *vastly different*. This strongly supports our earlier suggestion that the $H_{do}-L_{de}$ energy gap is not a reliable tool for predicting the relative reactivities of different dienes or dienophiles in IEDDACs.[8] By contrast, the $H_{de}-L_{do}$ energy gap for dienophiles **10**–**14** reasonably predicts their relative reactivities.

We can dismiss any significant steric effects to explain the large differences in reactivity among dienophiles **15**–**21** only by looking at the reactivity difference between dienophiles **18** and **20**. Clearly, **20** with its bulky *tert*-butyldimethylsilyl group would be expected to be unreactive if steric effects were dominant. Yet, it is more reactive than **18** and also **21**, which both possess a smaller $H_{do}-L_{de}$ energy gap!

Another striking observation is that the $H_{do}-L_{de}$ energy gaps of the unreactive electron-rich dienophiles **16**–**18** and **21** *are smaller* than the $H_{de}-L_{do}$ energy gaps of the reactive electron-deficient dienophiles **11**, **12**, and **13** as well as the energy gap between the diene's FMO (i.e. its dimerization). Again, this *unambiguously* confirms that these two frontier interactions affect the reaction rate differently. We would otherwise wrongly predict that dienophiles **16**–**18** and **21** should react more rapidly than dienophiles **11**–**13** with dienes **7** and **8**.

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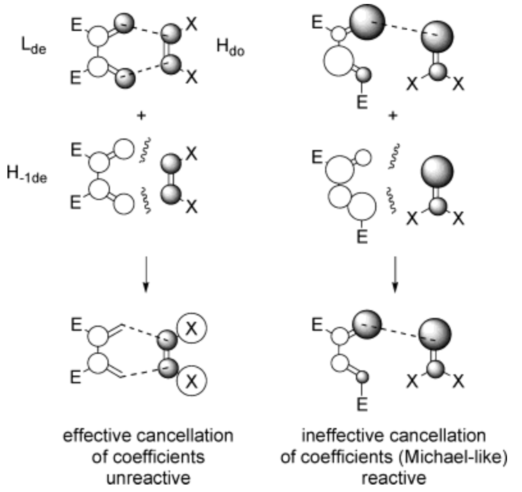

FIGURE 8. Symmetry leads to coefficient cancellation at transition state in the $H_{do}-L_{de}-(H\text{-}1)_{de}$ interaction.

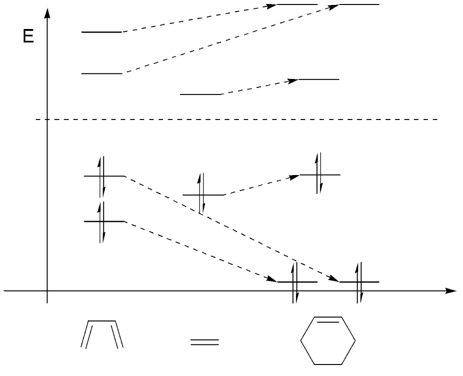

FIGURE 9. Energy diagram showing the fate of each frontier orbital in a perfectly synchronous Diels−Alder reaction (ethylene + butadiene).

However, and importantly, dienophiles **19** and **20** are reactive and **19** slightly more so than maleic anhydride (**10**) (entry 1, Tables 1 and 2). What makes these two dienophiles more reactive than their electron-rich homologues **15**−**18** and **21** with similar HOMO energies? The answer, we believe, lies in their pronounced polarization (dissymmetry): In synchronous or nearly synchronous Diels−Alder cycloadditions, the $H_{do}-L_{de}$ interaction suffers orbital coefficient cancellation at the transition state level (Figure 8) with the net result being that the $H_{do}-L_{de}$ affects mainly the formation of the π-bond in the cycloadduct (Figure 9).[4,7,8,25] Therefore, any change in the $H_{do}-L_{de}$ energy gap should result in a less pronounced effect on the reaction rate than a corresponding change in the $H_{de}-L_{do}$ energy gap, which is involved in the formation of a σ-bond of the final cyclohexene (Figure 9). This phenomenon could explain why variations in the energy of the H_{do} of symmetrically substituted dienophiles **14**, **17**, **18**, and **21** do not have much effect on their reactivities (cf. Table 3 and entries 5, 8, 9, and 12 in Tables 1 and 2). Moreover, examples of IEDDA reactions of symmetrical dienophiles are sparse in the literature, which may be indicative of their generally lower reactivities.[1b,26]

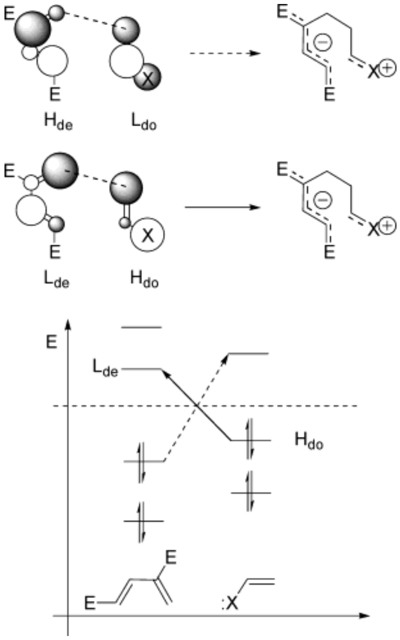

FIGURE 10. Vinyl ethers are better described as analogues of enolate anions than substituted ethylenes.

What, then, would make polarized dienophiles reactive in IEDDACs? The orbitals of a polarized electron-rich dienophile are perhaps better described by considering such dienophile as an analogue of an enolate anion rather than a substituted ethylene (Figure 10).[3a] A cycloaddition between an electron-poor diene and an electron-rich dienophile, taken to its extreme, could be considered as a Michael-type addition. In a full-fledged Michael addition, the most important (i.e. highly dominant) FMO interaction should be the HOMO of the nucleophile (the enolate anion) and the LUMO of the Michael acceptor (the electron-poor diene). Both FMOs are highly dissymmetric in terms of the relative size of their coefficients at each end-carbon of the diene and each carbon of the enolate anion (Figure 10). This highly dissymmetric interaction leads to the formation of a single σ-bond in the product.[3a,b] Therefore, in a highly asynchronous Diels−Alder transition state involving highly polarized IEDDAC partners, it is plausible that the $H_{do}-L_{de}$ interaction will be more like that of the $HOMO_{enolate}-LUMO_{electrophile}$ interaction of a Michael addition. The fate of the $H_{do}-L_{de}$ interaction in such highly asynchronous cycloadditions can no longer be purely that of becoming the product's π-bond but must involve some σ-bond formation and it will thus have more impact on the overall energy of the transition state. In other words, in IEDDAC, asynchronicity gives rise to a transition state reduced in energy compared to a synchronous one. To the best of our knowledge, no one has described the $H_{do}-L_{de}$ interaction in that manner before.

Good experimental evidence from our own work and that of others supports our hypothesis; symmetric dienophiles **17**, **18**, and **21** are unreactive despite a HOMO energy that should favor them over more reactive dieno-

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(25) This arises from a compulsory mixing of H_{do} with $H\text{-}1_{de}$ and L_{de} in an antibonding and bonding way, respectively. For a clear explanation of this phenomenon see: Woodward, R. B.; Hoffmann, R. In *The conservation of orbital symmetry*; Verlag Chemie: Weinheim, Germany, 1970; pp 21−30.

(26) Field, N. D. *J. Am. Chem. Soc.* **1961**, *83*, 3504−3507.

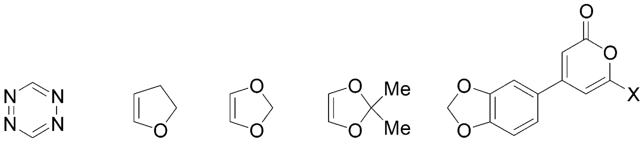

FIGURE 11. Dienes and dienophiles used in two separate reaction rates studies.

philes such as **16**, **19**, and **20**; the latter, dissymmetric, electron-rich dienophiles react faster with the dissymmetric diene **7** than with symmetric diene **8** (compare entries 7, 10, and 11 of each table); other observations extracted from the literature lend further support to our hypothesis: 1,2,4,5-tetrazine (**38**) reacts 18 times faster with **15** than with **18** and 6 times faster with **39** than with **40** (Figure 11);[27] pyrones **42** are reactive toward **19** but unreactive toward 2,2-dimethyl-1,3-dioxole (**41**) (Figure 11) despite HOMO energies close in value (−8.89 vs −8.69 eV, respectively);[28] EVE, 2,3-dihydrofuran, and other polarized electron-rich dienophiles were evidently more reactive than **41** as well as a host of other 1,2-alkoxyethenes (RO−CH═CH−OR) as dienophiles in the Lewis acid-catalyzed cycloaddition with α,β-unsaturated carbonyls.[29]

We offer that highly dissymmetric partners are *inherently more reactive* than symmetric ones in IEDDAC if the orbitals involved are of comparable energies and if steric effects are not impeding. In other words, 1,1-dialkoxyethenes (e.g. **19**) are inherently better dienophiles than 1,2-dialkoxyethenes (e.g. **18**). To the best of our knowledge, no report comparing the reactivities of dienophiles such as **19** and **18** has appeared in the literature.

Nonetheless, there are examples in the literature of IEDDACs where the reactivity trend can be explained based on the $H_{do}-L_{de}$ energy gap.[1b] This is not contrary to our present analysis since it suggests that within a series of highly polarized electron-rich dienophiles, the $H_{do}-L_{de}$ energy gap should be a reliable prediction tool.[30] The same could be true when comparing the relative reactivities of a series of symmetrical dienophiles. We are convinced that as more examples of IEDDAC are scrutinized in the present and future literature, the importance and value of dienophile polarization will be increasingly recognized.

Should coefficient size (i.e. polarization) also affect the reactivity of normal Diels−Alder cycloadditions? Much less so. The $H_{de}-L_{do}$ does not lead to coefficient cancellation in the product's occupied σ-orbital,[4,8,22] and this interaction already results in the formation of a σ-bond. Dissymmetry will neither impede nor help this situation.[31] For example, CEE (**11**) is slightly less reactive than maleic anhydride with diene **8** but slightly more reactive than maleic anhydride with diene **7** (cf. entries 1 and 2 in Tables 1 and 2). Dimethyl fumarate (**12**) has a similar reaction rate to its more polarized homologue **11** with both **7** and **8** (cf. entries 2 and 3 in Tables 1 and 2). However, Domingo and co-workers have shown that the highest acceleration in reaction rates comes from a nonsymmetrical substitution of ethylene. For example, 1,1-dicyanoethylene reacts with cyclopentadiene roughly 45 000 times more rapidely than acrylonitrile but tetracyanoethylene is only 1 000 times more reactive than 1,1-diacyanoethylene. Their calculation agreed well with experimental results, which were interpreted in terms of the local electrophilicity index ω_κ on each carbon of the substituted ethylenes.[10b] Whether the reaction of tetracyanoethylene is a true cycloaddition was, however, questioned.

Yet other NDAC reactions could proceed faster when highly polarized partners are involved. For example, Danishefsky-type dienes react with aldehydes to give dihydropyrans. It would be interesting to look at how dissymmetry on the diene affects the reaction rate in these cases.

Conclusions

The above experiments demonstrate the following: (a) The two frontier interactions in Diels−Alder cycloadditions are not equivalent. The $H_{do}-L_{de}$ should be used with caution when predicting the relative reactivities of dienes and dienophiles in IEDDA cycloadditions and the asynchronicity of the transition state should be taken into consideration. (b) In IEDDAC, polarized dienophiles are more reactive than nonpolarized ones and thus (c) orbital coefficients can be used to understand the relative reactivity and not only the regiochemistry of Diels−Alder cycloadditions. These demonstrations complement and support our previously reported hypothesis regarding the role that each frontier orbital plays in affecting the rates of Diels−Alder reactions.[8] Similar studies with other dienes and heterodienes are ongoing and will be reported in due course.

Experimental Section

Typical Procedure for Diels−Alder Reactions. To a solution of diene **7** or **8** (0.5 mmol) in dry toluene (3 mL in the case of **7** and 2 mL for **8**) under argon was added a dienophile (4 equiv for **7** and 2 equiv for **8**, except where indicated). The solution was then refluxed for the required time (see Tables 1 and 2). At the end of the reaction the solvent was evaporated and the crude purified by flash chromatography on silica. In one case, diene **7** was dissolved in ethyl vinyl ether (3 mL) and heated with a microwave oven at 150 W for 30 min (130 °C, 70 psi).

Where k_{rel} values are reported, aliquots of the reaction mixture were collected at 15- or 30-min intervals and the concentration of the starting diene or the cycloadduct was measured against an internal standard (chlorobenzene). Charts of $1/(a-b)\ln((b(a-x)/a(b-x))$ over time were used to extract the rate constants. Each reaction was done three times.

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[27] Sauer, J.; Heldmann, D. K.; Hetzenegger, J.; Krauthan, J.; Sichert, H.; Schuster, J. *Eur. J. Org. Chem.* **1947**, *12*, 2885−2896.

[28] Balazs, L.; Kadas, I.; Toke, L. *Tetrahedron Lett.* **2000**, *41*, 7583−7587.

[29] The former went at −78 °C while the other required 25 °C and higher catalyst loadings. See: Audrain, H.; Thorhauge, J.; Hazell, R. G.; Jorgensen, K. A. *J. Org. Chem.* **2000**, *65*, 4487−4497.

[30] See some examples in refs 1b and 27.

[31] Singleton and co-workers have calculated that unpolarized electron-poor dienophiles (acetylene dicarboxylate, dialkyl maleate, and triazolinediones) have a highly asynchronous transition state with nearly symmetrical dienes (isoprene or 2-*tert*-butyl-1,3-butadiene). Calculated asynchronous transition states were lower in energy than synchronous ones. They noted that reaction rates and kinetic isotope effects agreed with these results though experimental support for the calculated structures was notably ambiguous. Singleton, D. A.; Schulmeier, B. E.; Hang, C.; Thomas, A. A.; Leung, S.-W.; Merrigan, S. R. *Tetrahedron* **2001**, *57*, 5149−5160.

Adduct 22. The reaction was performed according to the general procedure starting with 196 mg of maleic anhydride. After evaporation, 240 mg of crude **22** (100%) was isolated. The product decomposed upon chromatography on silica gel. ^{1}H NMR ($CDCl_3$) δ 1.59−1.85 (m, 2H), 2.06−2.26 (m, 2H), 2.43−2.58 (m, 3H), 2.87 (d, 1H, $J = 13$ Hz), 3.58 (m, 1H), 3.84 (s, 3H), 4.48 (d, 1H, $J = 8.8$ Hz), 7.73 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 25.6 (t), 27.4 (t), 39.4 (t), 40.9 (d), 42.1 (d), 43.9 (d), 47.3 (d), 52.5 (q), 125.2 (s), 139.0 (d), 164.9 (s), 168.0 (s), 170.4 (s), 204.7 (s); IR (neat, cm^{-1}) 1781, 1733, 1275; LRMS (*m*/*z*) 278, 180, 121, 83; HRMS calcd for $C_{14}H_{14}O_6$ 278.0790, found 278.0794.

Adduct 23. The reaction was performed according to the general procedure starting with 345 mg of 1,1-dicarbethoxyethene. After evaporation of the solvents under reduced pressure, 180 mg of **23** (100%) was isolated. The product decomposed upon chromatography on silica gel. ^{1}H NMR ($CDCl_3$) δ 1.22 (m, 6H), 1.52−2.66 (m, 8H), 3.01−3.24 (m, 1H), 3.68, 3.73 (2s, 3H), 3.73 (m, 1H), 4.18 (m, 4H), 6.66, 6.70 (2m, 1H); IR (neat, cm^{-1}) 1725, 1623; LRMS (*m*/*z*) 352, 320, 292, 247, 219, 205, 191, 173; HRMS calcd for $C_{18}H_{24}O_7$ 352.1522, found 352.1529.

Adduct 24. The reaction was performed according to the general procedure starting with 288 mg of dimethyl fumarate. Conversion was 100% by NMR but the product decomposed upon chromatography on silica gel. ^{1}H NMR ($CDCl_3$) δ 1.3−1.5 (m, 1H), 1.6−1.87 (m, 1H), 1.9−2.1 (m, 2H), 2.2−2.4 (m, 2H), 2.5−2.7 (m, 2H), 3.05 (dd, 1H, $J = 11.4$ and 6.11 Hz), 2.89 (dd, 1H, $J = 11.4$ and 10.2 Hz), 3.65 (s, 3H), 3.69 (s, 3H), 3.80 (s, 3H), 6.72 (m, 1H); IR (neat, cm^{-1}) 1730, 1658; LRMS (*m*/*z*) 324 (M^+), 308, 292, 264, 232, 221, 205, 173; HRMS calcd for $C_{16}H_{20}O_7$ 324.1209, found 324.1212.

Adduct 26. The reaction was performed with a microwave oven (150 W for 30 min; 130 °C, 70 psi) in ethyl vinyl ether as solvent. After purification by chromatography on silica gel (dichloromethane:ether 95:5), 112 mg of **26** (89%) was isolated as a mixture of exo and endo isomers: ^{1}H NMR ($CDCl_3$) δ 1.17 (t, 6H, $J = 6.6$ Hz), 1.30−1.85 (m, 6H), 2.00 (m, 6H), 2.21−2.62 (m, 8H), 3.27 (m, 1H), 3.4−3.55 (m, 2H), 3.6−3.7 (m, 2H), 3.70 (s, 3H), 3.75 (s, 3H), 3.89 (m, 1 H), 6.43 (m, 1H), 6.48 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 15.3 (q), 15.4 (q), 22.5 (t), 22.8 (t), 31.1 (t), 31.3 (t), 32.0 (t), 34.9 (t), 37.3 (t), 38.0 (t), 40.2 (d), 40.5 (d), 45.9 (d), 50.8 (d), 52.0 (q), 52.3 (q), 64.3 (t), 64.6 (t), 74.5 (d), 74.5 (d), 128.3 (s), 130.4 (s), 140.4 (d), 142.4 (d), 170.9 (s), 172.0 (s), 199.4 (s), 200.8 (s); IR (neat, cm^{-1}) 1740, 1694, 1618; LRMS (*m*/*z*) 252 (M^+), 206, 180, 162, 147, 124, 121; HRMS calcd for $C_{14}H_{20}O_4$ 252.1361, found 252.1367.

Adduct 27. The reaction was performed according to the general procedure starting with 232 mg of 1,1-diethoxyethene. After purification by chromatography on silica gel (dichloromethane:ether 95:5), 134 mg of **27** (91%) was isolated as a single regioisomer. ^{1}H NMR ($CDCl_3$) δ 1.06−1.25 (m, 1H), 1.08−1.12 (t, 6H, $J = 6.7$ Hz), 1.45−1.51 (m, 1H), 1.66−1.84 (m, 1H), 1.85−2.1(m, 4H), 2.24−2.37 (m, 1H), 2.42−2.60 (m, 2H), 3.41−3.53 (m, 4H), 3.66 (s, 3H), 6.36 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 15.1 (q), 22.7 (t), 30.6 (t), 33.8 (t), 36.3 (d), 40.4 (d), 49.8 (t), 52.2 (q), 55.5 (t), 56.0 (t), 99.3 (s), 128.2 (s), 141.6 (d), 170.4 (s), 200.3 (s); IR (neat, cm^{-1}) 1736, 1691, 1628; LRMS (*m*/*z*) 296 (M^+), 251, 191, 163, 149, 134, 116; HRMS calcd for $C_{16}H_{24}O_5$ 296.1624, found 296.1619.

Adduct 28. The reaction was performed according to the general procedure starting with 436 mg of dienophile **20**. After purification by chromatography on silica gel (hexanes:ether 70:30), 70 mg of **28** (35%) was isolated as a single regio- and stereoisomer. Mp 115 °C; ^{1}H NMR ($CDCl_3$) δ 0.14 (s, 3H), 0.18 (s, 3H), 0.85 (s, 9H), 1.36−1.49 (m, 1H), 1.67−1.76 (m, 1H), 2.03−2.11 (m, 1H), 2.23−2.63 (m, 4H), 3.31 (s, 3H), 3.58 (s, 3H), 3.70 (m, 2H), 3.71 (s, 3H), 6.35 (m, 1H); ^{13}C NMR ($CDCl_3$) δ −4.1 (q), −1.8 (q), 18.9 (s), 22.7 (t), 26.1 (q), 27.2 (t), 40.3 (t), 42.8 (d), 48.9 (d), 52.4 (q), 53.7 (q), 61.6 (q), 83.2 (d), 100.0 (s), 127.5 (s), 139.8 (d), 170.4 (s), 200.0 (s); IR (neat, cm^{-1}) 1739, 1695, 1629; LRMS (*m*/*z*) 398, 353, 341, 309, 277, 235, 207, 189; HRMS calcd for $C_{20}H_{34}O_6Si_1$ 398.2124, found 398.2129.

Adduct 30. The reaction was performed according to the general procedure starting with 98 mg of maleic anhydride. After evaporation, 180 mg of crude **30** (100%) was isolated. ^{1}H NMR ($CDCl_3$) δ 2.62−2.68 (m, 2H), 2.98 (dd, 2H, $J = 18.7$, 2.2 Hz), 3.50 (m, 2H), 3.79 (s, 6H); ^{13}C NMR (CD_3COCD_3) δ 27 (t), 41.1 (d), 53.4 (q), 137.2 (s), 168.0 (s), 175.3 (s); IR (THF, cm^{-1}) 1783, 1732, 1275; LRMS (*m*/*z*) 237, 236, 163, 105; HRMS calcd for $C_{11}H_9O_6$ ($M^+ - OCH_3$) 237.0399, found 237.0393.

Adduct 31. The reaction was performed according to the general procedure starting with 172 mg of 1,1-dicarbethoxyethene. After purification by chromatography on silica gel (hexanes:ether 70:30), 142 mg of **31** (83%) was isolated. ^{1}H NMR ($CDCl_3$) δ 1.24 (t, 6H, $J = 6.6$ Hz), 2.17 (t, 2H, $J = 6.6$ Hz), 2.43 (m, 2H), 2.87 (m, 2H), 3.74 (s, 3H), 3.77 (s, 3H), 4.19 (q, 4H, $J = 6.6$ Hz); ^{13}C NMR ($CDCl_3$) δ 14.0 (q), 23.9 (t), 26.3 (t), 31.1 (t), 52.2 (q, 2 Me), 61.8 (t), 70.4 (s), 132.19 (s), 134.6 (s), 167.6 (s), 168.2 (s), 170.3 (s); IR (neat, cm^{-1}) 1734, 1658; LRMS (*m*/*z*) 310, 237, 209, 163, 137; HRMS calcd for $C_{15}H_{18}O_7$ ($M - CH_3OH$) 310.1052, found 310.1058.

Adduct 32. The reaction was performed according to the general procedure starting with 144 mg of dimethyl fumarate. Purification on silica gel with dichloromethane/ether (95/5) gave 142 mg of **32** (90%). Mp 108 °C; ^{1}H NMR ($CDCl_3$) δ 2.4−2.5 (m, 2H), 2.89−2.95 (m, 4H), 3.72 (s, 6H), 3.77 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 28.5 (t), 40.1 (d), 52.4 (q, broad), 133.2 (s), 167.5 (s), 173.7 (s); IR (neat, cm^{-1}) 1731, 1662; LRMS (*m*/*z*) 283 ($M^+ - OCH_3$), 250, 207, 163, 151; HRMS calcd for $C_{13}H_{15}O_7$ 283.0818, found 283.0808.

Adduct 33. The reaction was performed according to the general procedure starting with 86 mg of methyl acrylate. After purification by chromatography on silica gel (hexanes:ether 50:50), 39 mg of **33** (30%) was isolated along with 55 mg (32%) of dimer **37**. Compound **33**: ^{1}H NMR ($CDCl_3$) δ 1.66−1.74 (m, 1H), 2.06−2.13 (m, 1H), 2.30−2.46 (m, 1H), 2.48−2.51 (m, 4H), 3.70 (s, 3H), 3.76 (s, 6H); ^{13}C NMR ($CDCl_3$ δ) 23.8 (t), 25.8 (t), 28.0 (t), 37.9 (d), 51.9 (q), 52.2 (q), 133.0 (s), 135.4 (s), 167.9 (s), 168.5 (s), 174.5 (s); IR (neat, cm^{-1}) 1717, 1652; LRMS (C.I. NH_3, *m*/*z*) 272, 257, 225, 165, 137; HRMS calcd for $C_{12}H_{17}O_6$ (MH^+) 257.1025, found 257.1030.

Adduct 35. The reaction was performed according to the general procedure starting with 116 mg of 1,1-diethoxyethene. After purification by chromatography on silica gel (dichloromethane:ether 95:5), 119 mg of **35** (83%) was isolated. ^{1}H NMR ($CDCl_3$) δ 1.17 (t, 6H, $J = 7.7$ Hz), 1.87 (t, 2H, $J = 6.6$ Hz), 2.43 (m, 2H), 2.59 (br s, 2H), 3.50 (q, 4H, $J = 7.7$ Hz), 3.75 (s, 3H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 15.3 (q), 25.3 (t), 28.3 (t), 35.6 (t), 52.2 (q), 55.5 (t), 98.0 (s), 131.4 (s), 135.8 (s), 167.8 (s), 168.7 (s); IR (PhMe, cm^{-1}) 2995, 1728, 1726, 1653; LRMS (*m*/*z*) 286, 255, 209, 181, 139, 116; HRMS calcd for $C_{14}H_{22}O_6$ 286.1416, found 286.1418.

Adduct 36. The reaction was performed according to the general procedure starting with 218 mg of dienophile **20**. After purification by chromatography on silica gel (hexanes:ether 60:40), 111 mg of **36** (57%) was isolated. ^{1}H NMR (C_6D_6) δ 0.18 (s, 3H), 0.21 (s, 3H), 1.03 (s, 9H), 2.68−2.75 (m, 2H), 2.95 (m, 2H), 3.05 (s, 3H), 3.15 (s, 3H), 3.23 (t, 1H, $J = 3.5$ Hz), 3.42 (s, 3H), 3.48 (s, 3H); ^{13}C NMR ($CDCl_3$) δ −3.0 (q), 18.4 (s), 25.8 (q), 29.8 (t), 33.4 (t), 48.5 (q), 52.2 (q), 57.2 (q), 77.7 (d), 98.3 (s), 132.1 (s), 132.6 (s), 167.8 (s), 168.4 (s); IR (neat, cm^{-1}) 1731, 1721, 1261; LRMS (*m*/*z*) 388, 343, 299, 267, 218, 197, 193; HRMS calcd for $C_{18}H_{32}O_7Si_1$ 388.1917, found 388.1909.

Dimer 37. The reaction was performed according to the general procedure with no dienophile starting with 85 mg of **8**. After purification by chromatography on silica gel (hexanes: ether 95:5), 61 mg of **37** (72%) was isolated. ^{1}H NMR ($CDCl_3$) δ 2.12−2.19 (m, 3H), 2.37−2.45 (m, 1H), 2.58 (d, 1H, $J = 18.7$ Hz), 2.87 (dd, 1H, 18.7, $J = 3.0$ Hz), 3.67 (s, 3H), 3.73 (s, 3H), 3.74 (s, 3H), 3.78 (s, 3H), 5.74 (s, 1H), 6.42 (s, 1H); IR (neat, cm^{-1}) 3000, 2958, 2847, 1726, 1657, 1627, 1435, 1259, 1075; ^{13}C NMR ($CDCl_3$) δ 23.4 (t), 26.8 (t), 34.2 (t), 46.9 (q), 52.2 (q), 52.3 (q), 52.5 (q), 65.8 (s), 126.3 (d), 128.5 (s), 133.5 (s), 139.9 (s), 166.2 (s), 167.8 (s), 168.2 (s), 174.4 (s); LRMS (C.I. NH_3

m/*z*) 358 (MNH_4^+), 341 (MH^+), 309, 294, 249, 221, 189; HRMS calcd for $C_{15}H_{16}O_7$ ($M - CH_3OH$) 308.0896, found 308.0905.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra of compounds **8**, **22**, **26**−**28**, **30**−**33**, and **35**−**37** in addition to ^1H NMR of **7**, **23**, and **24**; calculation details are included. This material is available free of charge via the Internet at http://pubs.acs.org.

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