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A QUANTITATIVE ANALYSIS OF THE CHARGE-TRANSFER PERTURBATION MODEL FOR THE CYCLOADDITION OF DIAZOALKANES WITH OLEFINS.

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Abstract - Non-frontier charge-transfer interactions have been investigated for the cycloaddition of diazomethane, 2-diazopropane and methyl diazoacetate to a wide group of mono and disubstituted olefins. The main result is that these interactions, far from beeing negligible, play a decisive role in the rationalization of both the regiochemistry and the rate of these reactions.

INTRODUCTION

A recent book[1] on the chemistry of 1,3-dipolar cycloaddition summarizes the most important conclusions about this class of reactions. Extensive rationalization of the most interesting aspects, i.e. regiochemistry and reaction rate, rests firmly on perturbation molecular orbital (PMO) methods [2-5] and, mainly, on its frontier orbital (FO) approximation.

However the practical use of FO theory has reached such a high degree of "versatility" as to account for whatever experimental result one has to handle. After all, the regiochemical problem is only a black-or-white (or grey, i.e. mixture) problem and a very large number of options can be selected which may switch predictions from one to the other: one could use plain FO coefficients or the squared products of FO coefficients and appropriate interaction integrals, one could take coefficients from different LCAO approximations, one could pick out different orbitals as the "true" FO, or simply assign the useful relevance either to one non-FO or to the other frontier interaction (e.g. HO_{DP}-LU_{DF} and a bit of LU_{DP}-HO_{DF}, DP = dipole, DF = dipolarophile); one could or could not introduce d-orbitals, and even use figures (coefficients?) obtained as the average of coefficients calculated with and without d-expansion.[6] Moreover, ionization potentials and electron affinities, or their various estimates, may replace calculated orbital energies; also weighted averages of first and second ionization potentials have been taken as HO energies.[7] Lastly, different kinds of secondary interactions, steric and electrostatic factors may or not be ignored. Consequently, it is not surprising that new regiochemical results produced in the last decade have been found to agree with FO theory and so to support it.

In our opinion, even if some of these adjustments are reasonably justified, the practice of their non-systematic use can only result in weak explanations and uncertain predictions.

On the other hand, one cannot ignore that Bastide and Coll.[8] had shown, extensively, that the complete change-transfer term can account for regiochemistry with a success that is, at least, comparable to that of FO theory.

On the side of reaction rates, the most impressive match between experimental data and their theoretical counterparts concerns diazoalkanes, and mainly diazomethane cycloadditions, and is due to the extensive investigation of Huisgen, Sustmann and Coll. The up-to-date conclusions are:

i) the FO approximation (HO_{DZM}-LU_{DF}) fails to correlate the reaction rate of a series of conjugated olefins,[9]

ii) the inclusion of other interactions involving non-frontier unoccupied MO's of alkenes[9] does succeed in giving the requested linear correlation (log k_2 vs. $\Sigma_i[HO_{DZM}-U_{i,DF}]$, r^2=0.86);

iii) a further approximation to the FO model, that consists in ignoring the changes of MO coefficients along the series of olefins, leaving the exclusive role of ordering reaction rates to the inverse of the frontier energy gaps, obtains a good linear relationship for DZM (r^2=0.90);[10] in this correlation the energy gaps are based on the experimental IP's and empirically evaluated EA's.

iiii) linear correlations of log k_2 for type II 1,3-dipoles (e.g. methyl diazoacetate) have not yet been achieved through approximation iii);[11a]

iiiii) U-shaped relationships of log k_2 vs. dipolarophile ionization potentials have been obtained for several type II 1,3-dipoles,[11b,c] and shown to be consistent with the above approximation iii): the U curve is interpreted as the sum of the two frontier contributions, the HO_{DP}-LU_{DF} predominating in the right-branch and the LU_{DP}-HO_{DF} becoming the dominant one in the left-branch where electron-rich reactants are plotted. The poor quality of U curves is only a minor drawback.

A few comments are necessary. Certainly results iii) and iiiii) could be read as successes of FO theory, but one ought to: a) accept that the trend of MO coefficients, necessary for explaining regiochemistry, must be necessarily ignored to account for reaction rates; b) be willing to believe that sooner or later the missing correlations iiii) will be obtained, and that, on the contrary, c) the extant correlation ii) is incidental.

The above survey and criticisms strongly recommend further investigation: both aspects of cycloaddition, regiochemistry and reaction rate, should be dealt with a single, rigid (i.e. without non-systematic options for single cases) procedure either in the FO scheme or in the complete charge-transfer model.

In the present paper we explore the effects of molecular distortions, according to a suggestion by Klopman,[12] on the FO performance; then we analyze the role of non-FO interactions, also introducing a systematic empirical reduction of the orbital energy gaps, in the undistorted molecules.

METHODS, MOLECULES AND DATA

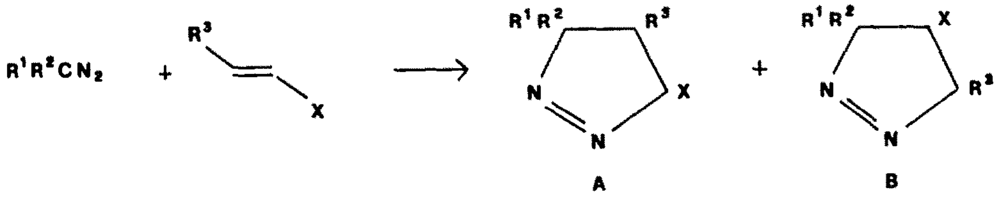
MO energies and coefficients for PMO calculations are standard CNDO/2 quality; this choice rests on the following arguments: a) literature and experience show that the insufficient quality of CNDO/2 calculations is not the real cause of disappointing results with FO theory in this field; b) standard CNDO/2 FO energies do not reproduce the experimental ionization potentials and electron affinities, but the same is true also for minimal basis ab-initio calculations. Actually, there is no good reason to expect this result, except for the highest occupied MO (Koopman's approximation);

c) since our work concerns a widely investigated area, where CNDO/2 has been in common use, the adoption of the very same procedure favours the comparison with previous calculations; d) the ortho-normality condition $C^{+}C=1$, explicitly required by Salem's model[2] is fulfilled by CNDO procedure.

For treating distorted molecules a computer program was assembled for obtaining MO's using a basis of hybrid atomic orbitals (HAO)[13,14] and the CNDO/2 parametrization.

The molecules in study comprehend three 1,3-dipoles, diazomethane (DZM), 2-diazopropane (DZP), and methyl diazoacetate (DZA), and about twenty dipolarophiles, ethene, mono and polysubstituted alkenes, bearing strong acceptor ($-NO_2$, $-CO_2Me$) and strong donor (-pyrrolidinyl) substituents, conjugated groups ($-CH=CH_2$, -Ph), sulphonyl groups both in open and cyclic structures. The complete list is given in Table 4.

Let us call A and B the two possible adducts from cycloaddition, and let X be the substituent bearing heteroatoms in polysubstituted alkenes.



Only regioisomer A was, as a rule, detected in the reactions of DZM; mixtures were found only for propene,[15] thiete 1,1-dioxide,[16] and styryl sulphones.[17,21] Ethyl vinyl ether gave A[18] and N-isobutenyl pyrrolidine did not react.[19] DZA cycloaddition led to B with N-isobutenylpyrrolidine and N-(1-cyclopentenyl)pyrrolidine,[20] whereas the regiochemistry with ethyl vinyl ether has not yet been reported.[21] Relative cycloaddition rate constants for DZM and DZA are taken from ref. 9 and 10, and ref. 11c and 11d, respectively.

Charge-transfer energies. Salem's expression[2] for the energy of charge-transfer interaction k between an occupied orbital i and a vacant one j are:

$$-CT^{A}_{k}=2(C_{C}C_{\beta}\gamma_{CC} + C_{N}C_{\alpha}\gamma_{CN})^{2}/|\Delta\epsilon| \qquad \text{for adduct A}$$

$$-CT^{B}_{k}=2(C_{C}C_{\alpha}\gamma_{CC} + C_{N}C_{\beta}\gamma_{CN})^{2}/|\Delta\epsilon| \qquad \text{for adduct B}$$

where $|\Delta\epsilon|=|\epsilon_i-\epsilon_j|$ is the orbital energy gap, C_C and C_N are the π-coefficients of the terminal atoms of 1,3-dipole in i(j), C_α and C_β are the π-coefficients of the olefinic α and β carbon atoms in j(i). The interaction integral γ cannot be estimated satisfactorily and must be treated as an empirical parameter; it appeared reasonable[22] to assume the same rules as those adopted in CNDO/2 for the evaluation of core resonance integrals ($\beta_{xy}=\beta^{\circ}_{xy}S_{xy}$, $\beta^{\circ}_{CC}=-21$ eV, $\beta^{\circ}_{CN}=-23$ eV), where S_{xy} is the overlap integral between the π-AO (or π-HAO in distorted molecules) of the reacting centers at a distance of 2.5 Å. It may be added that all the conclusions to be reached are largely independent of the actual values adopted for this distance, in the range of the reasonable values of 2-3 Å. Single charge-transfer interactions can be summed up into various contributions,

$HO_{DP}-LU_{DF}$; $LU_{DP}-HO_{DF}$	frontier contributions
$\Sigma_{j}HO_{DP}-U_{j,DF}$	contribution of dipole HOMO as a donor
$\Sigma_{ij}O_{i,DP}-U_{j,DF}$	total contribution of dipole as a donor
$\Sigma_{ij}U_{j,DP}-O_{i,DF}$	total contribution of dipole as an acceptor
$E_{CT}=\Sigma_{k}CT_{k}=\Sigma_{ij}O_{i,DP}-U_{j,DF}+\Sigma_{ij}U_{j,DP}-O_{i,DF}$	total charge-transfer energy

that have chemical meaning in the charge-transfer model. For each contribution a regiochemical index D_{B-A} can be calculated as the difference between the values for adduct B and A ($E_{CT,B}-E_{CT,A}$).

Geometries of 1,3-dipoles. Bond lengths C-N, N-N, C-H were fixed at the experimental values of DZM,[23] 1.30 Å, 1.139 Å, 1.075 Å respectively. Bond angles were given calculated values, optimized according to STO-3G calculations; these are HCH (DZM): 123.3° (planar), 126° (exp.), 120.8° (20° distorted), 117.9° (30° distorted); CCC (DZP): 122.8° (planar); HCC (DZA): 119.9° (planar); this choice allows for a single criterion for molecules with known and unknown geometries and for distorted molecules. Other bond lengths were assumed from propene, C-Me 1.506 Å, C-H for Me 1.117 Å, and from methylacrylate, $C-CO_2Me$ 1.44 Å, C=O 1.21 Å, C-O 1.36 Å, O-Me 1.41 Å.

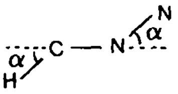
Geometries of dipolarophiles. Bond lengths for ethene are experimental values: C=C 1.336 Å, C-H 1.089 Å; bond angles, from STO-3G optimization, are: HCH 116.1° (planar), 116.2° (exp.), 116.5° (30° distorted). Geometrical data for substituted alkenes were either experimental or standard values,[23] bond angles for open systems have been empirically optimized by imposing direct valence condition to the hybridization procedure (atom-following).[14]

RESULTS AND DISCUSSION

FO analysis in distorted molecules. According to Klopman,[12] FO's gain an increasing weight during the molecular distortion in the direction required to complete the reaction, so that MO calculations on distorted, isolated molecules are able to single out the stereodirecting orbital(s) i.e. "the orbital(s) that concentrates in the region of the bond to be formed and whose energy is decreased most". If supported by actual calculations, this procedure could supply FO theory with a rigid choice of the true FO orbitals and demonstrate their almost exclusive role in determining both the regiochemistry and the correlations with the reaction rates. Extensive calculations (STO-3G and CNDO/2) on distorted molecules have been done, but they will not be reported here in detail; the main conclusions are:

a) the frontier orbital energy narrowings caused by distortion are modest and unselective; as an example the frontier orbital energy gaps for the reaction of diazomethane (DZM) and ethene are reported in Table 1; both $HO_{DP}-LU_{DF}$ and $LU_{DP}-HO_{DF}$ distances are decreased owing to stabilization of

Table 1. Frontier orbital energy gaps (eV) for the reaction of diazoalkanes with ethene.

		DZM			DZA	DZP
						
		$\alpha = 0°$	$\alpha = 20°$	$\alpha = 30°$	$\alpha = 0°$	$\alpha = 0°$
STO-3G	$-(\epsilon_{HO,DP}-\epsilon_{LU,DF})$	15.48	15.02	14.55	15.79	14.49
	$\epsilon_{LU,DP}-\epsilon_{HO,DF}$	16.77	16.05	15.29	14.71	17.00
	Δ	1.29	1.03	0.74	-1.08	2.51
CNDO/2	$-(\epsilon_{HO,DP}-\epsilon_{LU,DF})$	16.57	15.97	15.43	16.75	15.04
	$\epsilon_{LU,DP}-\epsilon_{HO,DF}$	20.60	19.85	19.03	18.60	20.14
	Δ	4.03	3.88	3.60	1.85	5.10
Exp. or	$IP_{DP}-EA_{DF}$	10.78			10.98	
Estimated[a]	$-EA_{DP}+IP_{DF}$	12.31			11.51	
	Δ	1.53			0.53	

a) IP: DZM = 9.00[24], DZA = 9.20[19,20a], Ethene = 10.51[25]
EA: DZM = -1.80[26], DZA = -1.00[19,20a], Ethene = -1.78[27]

Table 2. CNDO/2 energies (ϵ) and coefficients (C_α, C_β) of unoccupied molecular orbitals of trans-phenyl styryl sulphone and corresponding charge-transfer energies and regiochemical indices (D_{B-A}) of their interactions with diazomethane HOMO.[a]

Planar					Distorted (30°)				
ϵ(eV)	C_α	C_β	E_{CT} (kJmol^{-1})	D_{B-A}	ϵ(eV)	C_α	C_β	E_{CT} (kJmol^{-1})	D_{B-A}
5.52	.44	-.55	-30.94	2.18	4.99	.26	-.37	-21.90	3.34
2.37	.39	-.28	-18.16	-2.33	2.59	.35	-.23	-22.39	-3.67
1.70	.30	-.30	-14.66	0.01	0.98	.39	-.40	-43.68	0.52

a) C_α : double bond carbon atom bound to the sulphonyl group; D_{B-A}: regiochemical index, i.e. the charge-transfer energy difference between the value for adduct B (4-sulphonyl pyrazoline) and A (3-sulphonyl pyrazoline) $[E_{CT,B}-E_{CT,A}]$; a negative value favours regioisomer B.

Diazomethane HOMO:linear, ϵ =-11.21 eV, C_C=.75, C_N =-.65; distorted, ϵ =-11.19 eV C_C= .73 C_N=-.61

LU energies, so that the role of the former frontier interaction is not enhanced by distortion. Frontier orbital energy gaps for methyl diazoacetate (DZA) and 2-diazopropane (DZP) with ethene have been reported in Table 1 for further considerations.

b) The FO coefficients of the π-type hybrid atomic orbitals (π-HAO) of DZM and ethene are decreased by distortion; in substituted alkenes HO coefficients undergo non systematic changes; on the contrary the LU coefficients are systematically increased in electron-deficient dipolarophiles and decreased in electron-rich ones: this behaviour implies that distortion increases (reduces) the importance of HO_{DP}-LU_{DF} interaction with electron withdrawing (releasing) substituents, which seems quite reasonable. Moreover, in those cases where more than one unoccupied MO is candidate as LU (e.g. in electron-deficient and/or conjugated dipolarophiles), the increased importance of a certain interaction can provide a criterion for detecting the "true" LU. The criterion has been adopted for some intriguing cases as sulphones; trans-phenyl styryl sulphone is shown in Table 2 as an example.

In the planar calculation the third-LU (first row of Table 2) of trans-phenyl styryl sulphone gives the highest CT stabilization and favours 3-sulphonyl pyrazoline, the second-LU an intermediate CT energy and 4-sulphonyl pyrazoline, whereas the first LU gives the lowest charge-transfer energy and favours a mixture of the two adducts. By effect of distortion, the first LU gains a lower energy and higher coefficients so as to become the most important, and its regiochemical index points out a mixture, in agreement with the experiment.[17,21] The Table also shows that distortion does not alter orbital polarizations.

c) an overall increase of CT energies on distortion, but for those orbitals where coefficients decrease largely, is due to the increased interaction overlaps of the π-HAO's with respect of those of the pure π-AO's of the planar reactants.

Apart from some aspects of conclusion b), the procedure gives disappointing results, especially as concerns the justification for ignoring non-frontier interactions and the alternative FO interaction (LU_{DP}-HO_{DF}), involving diazomethane as an acceptor.

Moreover application of FO model to DZM cycloadditions by using MO's of distorted molecules does not improve the correlation between rate constants and CT energies as clearly shown in Figure 1.[28]

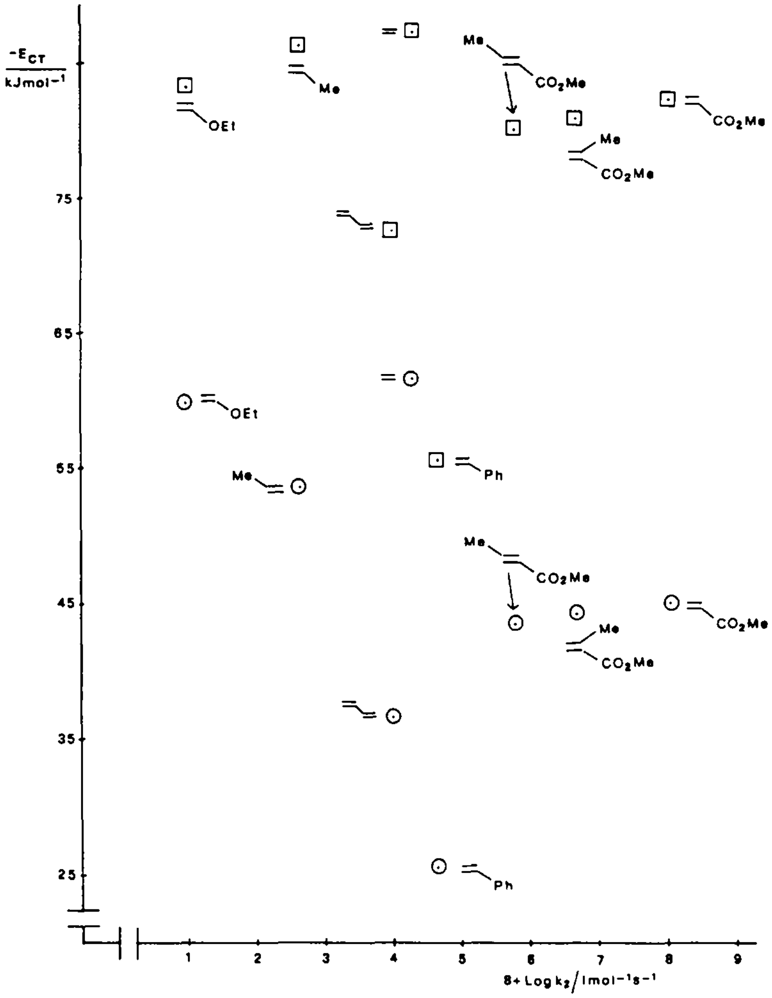


Figure 1. Frontier charge-transfer energies [HO diazomethane-LU dipolarophiles] vs. rate constants for distorted (□) and undistorted molecules (○).

Total charge-transfer stabilizations (undistorted molecules). A different way to gain rigidity in predictions is to sum up all the interactions, in obedience to the common place that all that is negligible can be added without damage.

The total charge-transfer stabilization for diazomethane cycloaddition shows an excellent correlation with log k_2 (Figure 2); it is interesting to observe that N-isobutenylpyrrolidine, in agreement with experiment, is reckoned to be non reactive.

Figures in parentheses represent the total regioselectvity index i.e. the total CT stabilization differences between B and A adducts, so that positive numbers mean that A is predicted. As far as regiochemistry is concerned the following indexes (kJmol^{-1}) regarding the six sulphones, not present in Figure 2, can also be added.

$CH_2{=}CHSO_2Ph$ 1.00; $MeCH{=}CHSO_2Ph$ 1.01; $MeCH{=}CHSO_2Me$ 1.11; $PhCH{=}CHSO_2Ph$ 0.33; $PhCH{=}CHSO_2Me$ 0.32; thiete 1,1-dioxide 0.36.

They conform to the experimental findings, that is mixtures for the last three compounds and A adducts for the first three.

The analogous plot for methyl diazoacetate cycloaddition, indicate a good linearity for all the dipolarophiles, but for N-isobutenylpyrrolidine and N-(1-cyclopentenyl) pyrrolidine. The

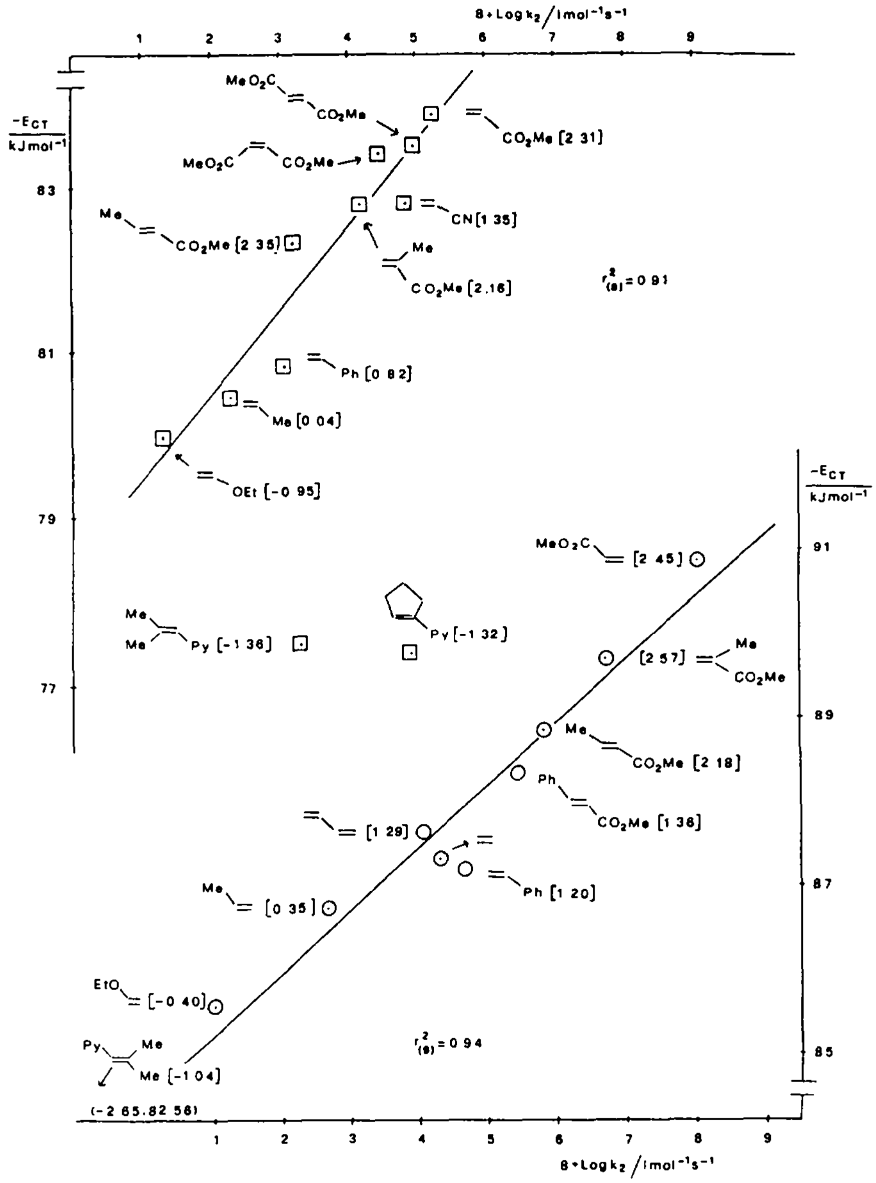


Figure 2. Correlation between total charge-transfer energies and rate constants for the cycloaddition of diazoalkanes to olefinic dipolarophiles.
☐ Methyl diazoacetate; ○ Diazomethane; Py= pyrrolidinyl

calculated regioselectivity assignes A adducts to electron deficient dipolarophiles and B adducts to electron-rich ones, which appears to agree with experiment. The lower reactivity of DZA with respect to DZM is also accounted for.

In spite of the reasonable success of the straightforward application of the PMO theory (standard CNDO/2 energies and coefficients), theoretical results point out also some enlightening deficiencies: a) in DZA cycloaddition, calculations fail to account for the fairly high reactivity of enamines; as these are the only examples falling within the left-branch of the U-curve, it ought to be concluded that for all the reactions involving dipolarophiles falling within this region the reaction rate would be wrongly predicted; b) in DZM cycloaddition the regiochemistry of ethyl vinyl ether is missed; c) calculation (not reported) show that 2-diazopropane cycloadditions proceed slower than those of DZM, whereas the opposite is found in experiments, at least when steric hindrance is not overhelming.[29a]

The above shortcomings a) and b) can be traced back to an insufficient relative weight of the contribution $\Sigma_{ij}U_{j,DP}-O_{i,DF}$ the contribution of DP acting as an acceptor. In fact, resorting to the interpretation of the U-curves, these interactions, or their frontier component, should be responsible for the high reactivity of DZA with electron-rich dipolarophiles which is not accounted for in the above calculation; furthermore, since this contribution favours adduct A in the reaction between ethyl vinyl ether and DZM, its underestimation might be responsible for the wrong, B, prediction of stereochemistry. Shortcoming c), on the other hand, can be due to underestimation of the other contribution, $\Sigma_{ij}O_{i,DP}-U_{j,DF}$, where DP acts as a donor; in fact, the decreased HO-LU energy gap in DZP + ethene with respect to DZM + ethene (see Table 1) is not sufficient to account for the higher reactivity of DZP, because it is counteracted by the overall decrease in MO coefficient values ($HOMO_{DZM}$: $C_C = 0.75, C_N=-0.65$; $HOMO_{DZP}:C_C=0.69$, $C_N=-0.61$).

Inspection of Table 1 appears to corroborate the above arguments: the frontier orbital energy gaps are much higher than the experimental (or estimated) differences between ionization potentials and electron affinities. If these empirical differences are admitted to be more suitable to represent the energy gaps governing the charge-transfer processes than those calculated from frontier orbital energies,[29b] it comes out that both contributions, in the above calculation, are underestimated. Empirical reduction parameters X, Y could be introduced in the calculated FO energy differences to reproduce the empirical ones:

$[\epsilon_{HO,DP}-\epsilon_{LU,DF}]-X$ $\qquad$ $[\epsilon_{LU,DP}-\epsilon_{HO,DF}]-Y$.

For DZM+ ethene and CNDO/2 calculation, X and Y amount to be 0.2128 au (5.79 eV) and 0.3047 au (8.29 eV) respectively. Quite similar values are obtained for DZA+ ethene [X=0.2120 au (5.77 eV), Y=0.2606 au (7.09eV)]. For DZM+substituted alkenes the values of X and Y fall within the ranges 0.17-0.20 au (4.63-5.44 eV) and 0.21-0.25 au (5.71-6.80 eV) respectively. To avoid a large number of reduction parameters and/or a systematic use of experimental values (often unavailable), we have tried X=0.20 au (5.44 eV) and Y=0.30 au (8.16 eV) for all the diazoalkanes reacting with ethene, and substituted ethenes, both for frontier and non-frontier interactions; however, a slight distinction for mono and disubstituted olefins within the X range found above [X=0.18 au (4.90 eV) and X=0.17 au (4.63 eV) respectively], was introduced to correct some minor systematic scatter. Although the introduction of empirical corrections always involves some arbitrariness, we feel that our choice is a reasonable and rigid way to overcome the deficiencies discussed above.

The results reported in Figure 3 show that all the shortcomings of Figure 2 are eliminated: the relationship of DZM is still a very good one, ethyl vinyl ether reaches a positive, small, regiochemical value, N-isobutenylpyrrolidine being still unreactive; N-isobutenyl pyrrolidine and N-(1-cyclopentenyl)pyrrolidine assume now a correct location in the reactivity sequence with DZA; moreover, DZP tends to be more reactive than DZM whereas DZA is still less reactive. This last conclusion can be demonstrated by the results of Table 3 where a few examples are reported.

Table 3. Total CT stabilization energies ($-E_{CT}$/kJmol^{-1}) ($\Delta\epsilon$ reduced)

	$CH_2=CHCO_2Me$	$CH_2=CH_2$	$CH_2=CHMe$	$CH_2=CHOEt$
DZA	127.68	124.24	122.07	121.92
DZM	139.19	134.27	131.14	129.44
DZP	141.12	135.20	131.85	130.15

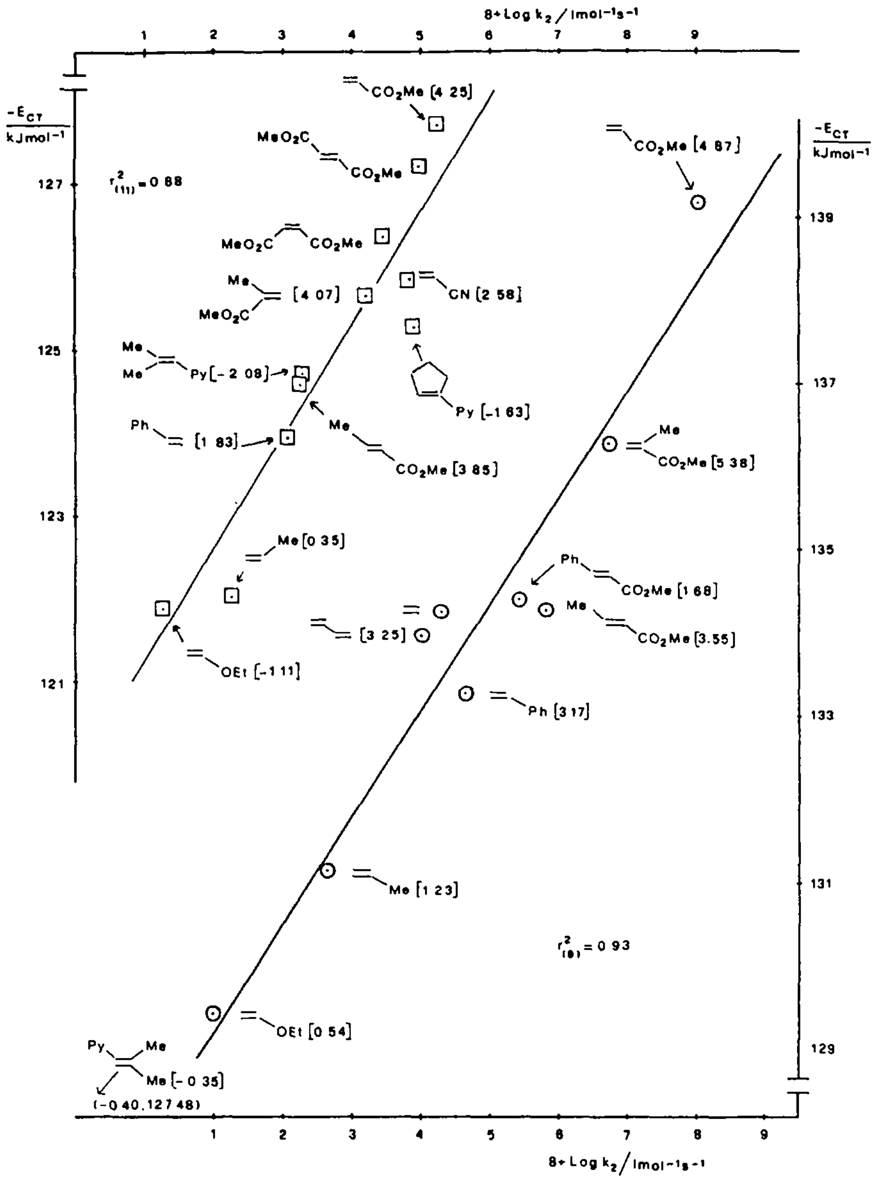


Figure 3. Correlation between total charge-transfer energies (Δ ε reduced) and rate constants for the cycloaddition of diazoalkanes to olefinic dipolarophiles.
☐ Methyl diazoacetate; ○ Diazomethane; Py= pyrrolidinyl

In Table 4 the evolution of charge-transfer energies (all the E_{CT} values refer to the adducts calculated to be favoured), and regiochemical indexes (D_{B-A}) from the frontier approximation to the complete term is reported.

The agreement between the regiochemical index from the dominant FO interaction (column 2) and the experimental regiochemistry (column 14) is impressive, with the only famous exception of ethyl vinyl ether; however, let us underline that this frontier interaction succeeds in giving the correct regiochemistry even when it represents a mere 3-4% (column 3) of the total charge-transfer energy. The results of column 1 confirm the lack of correlation between the dominant FO interaction energy and the reaction rate. It is significant that the progressive inclusion of further interactions, with unoccupied MO's of the dipolarophiles (columns 4-9), while building up the

Table 4-Charge-transfer interaction analysis for the reaction of diazomethane with olefines.

	Frontier HO_{DZM} LU_{DF}			$\sum_{j=1}^{2} HO_{DZM} - U_{j,DF}$		$\sum_{j=1}^{3} HO_{DZM} - U_{j,DF}$		$\Sigma_j HO_{DZM} - U_{j,DF}$		$\Sigma_{ij} O_{i,DZM} - U_{j,DF}$		Total CT		Experimental
	$-E_{CT}$	D_{B-A}	%	$-E_{CT}$	D_{B-A}	$-E_{CT}$	D_{B-A}	$-E_{CT}$	D_{B-A}	$-E_{CT}$	D_{B-A}	$-E_{CT}$	D_{B-A}	A%
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
$CH_2=CH_2$	91.92		68					91.92		92.04		134.27		
$CH_2=CHMe$	77.39	1.67	59	86.66	-0.47			86.66	-0.47	86.91	-0.41	131.14	1.23	87[d]
$CH_2=CHPh$	39.33	5.78	30	83.51	2.46	88.17	1.29	88.17	1.29	88.68	1.27	133.28	3.17	100[e]
$CH_2=CHCH=CH_2$	55.60	6.60	42	89.27	1.50			89.27	1.50	89.83	1.47	133.96	3.25	100[f]
$CH_2=CHCO_2Me$	70.04	10.22	50	97.76	5.29	98.91	5.08	99.06	5.05	99.74	4.79	139.19	4.87	100[g]
$CH_2=CHCN$	78.05	6.69	57	95.37	2.62			95.37	2.62	95.88	2.50	136.77	3.36	100[g]
$CH_2=CHNO_2$	47.38	8.68	33	106.68	5.54			106.68	5.54	107.12	5.24	142.70	4.59	
$CH_2=CHSO_2Ph$	4.35	0.82	3	67.32	2.87	98.89	2.27	99.66	2.11	99.78	1.96	139.73	1.80	100[h]
$CH_2=CHOEt$	85.04	-3.01	66	85.06	-3.02	85.13	-3.03	85.22	-3.04	85.24	-2.80	129.44	0.54	100[i]
$MeCH=CHCO_2Me$[b]	66.08	8.95	49	77.71	4.56	91.09	5.72	93.72	5.49	94.56	5.17	134.27	3.55	100[g]
$MeCH=CHNO_2$[b]	47.82	8.37	35	90.23	3.18	101.40	5.30	101.40	5.30	102.08	4.98	137.79	2.75	
$PhCH=CHCO_2Me$[b]	51.77	2.08	39	62.47	6.85	85.31	3.04	93.73	3.95	94.80	3.69	134.40	1.68	100[n]
$PhCH=CHNO_2$[b]	49.12	3.72	36	93.69	5.09	98.97	6.15	99.25	4.73	100.03	4.40	135.84	1.75	
$CH_2=CMeCO_2Me$	66.92	9.69	49	82.50	7.28	93.76	4.01	93.76	4.01	94.59	3.84	136.28	5.38	100[m]
$MeCH=CHSO_2Ph$[b]	5.88	1.01	4	76.17	2.09	86.58	1.40	95.44	3.17	95.66	2.92	135.13	1.07	100[h]
$MeCH=CHSO_2Me$[b]	6.14	1.02	4	79.59	2.57	89.26	1.94	97.91	3.62	98.14	3.33	137.28	1.19	100[h]
$PhCH=CHSO_2Ph$[b]	22.93	0.02	17	46.99	-3.56	89.89	0.37	94.94	1.69	95.35	1.50	135.74	-0.48	40[h]
$PhCH=CHSO_2Me$[b]	28.06	-0.18	21	52.85	-3.26	92.03	0.92	97.47	2.02	97.89	1.82	136.73	-0.54	25[h]
Thiete 1,1-dioxide	97.95	-0.03	68	103.30	1.68	104.62	1.60	104.62	1.60	104.89	1.46	144.75	0.15	60[q]
N-isobutenylpy[c]	65.17	-5.76	51	65.18	-5.76	66.55	-6.05	77.43	-3.31	77.85	-3.09	127.48	-0.35	
N-(1-cyclopentenyl)py[c]	64.46	-3.27	50	65.33	-3.26	65.77	-3.71	79.34	-4.42	79.73	-4.06	129.62	2.04	
Methylfumarate	66.63		48	66.88		100.66		101.11		102.41		139.62		
Methylmaleate	65.39		47	65.57		76.97		99.43		100.50		138.34		

a) Energy value in $kJmol^{-1}$; b) Trans; c) py=pyrrolidinyl; d) Ref. 15; e) Ref. 30; f) Ref. 31; g) Ref. 32; h) Ref. 17; i) Ref. 18; m) Ref. 33; n) Ref. 34; q) Ref. 16

Table 5. Percentage of DP (donor)⟶DF (acceptor) contribution over the total CT energy.

	$CH_2=CHCO_2Me$	$CH_2=CH_2$	$CH_2=CHPh$	$CH_2=CHMe$	$CH_2=CHOEt$	$PyCH=C(Me)_2$
DZM	71.6	68.5	66.5	66.3	65.9	61.0
DZA	67.7	64.4	62.3	62.1	61.1	54.7

correlation between rate constants and charge-transfer energies (log k_2 vs. $\Sigma_j HO_{DP}-U_{j,DF}$, r^2 = 0.88, n=9), destroys the overall agreement with the experimental regiochemistry. In fact the regiochemistry according to column 9, i. e. summing up the contributions where diazomethane acts as a donor through its HOMO, is unsatisfactory mainly because it does not account for the mixtures. The inclusion of DZM second-HOMO gives only minor contributions (compare columns 8 and 9 with 10 and 11; see also Ref. 9).

By contrast the complete calculation accounts for the regiochemistry satisfactorily (column 13 vs. 14); the comparison of columns 11 and 13, shows that this is the result of the contribution of the interactions where diazomethane acts as an acceptor, $\Sigma_{ji} U_{j,DZM}-O_{i,DF}$; as can be seen also from columns 10 and 12, these interactions are far from being negligible!

Certainly the correlations reported in Figure 3 are empirically adapted, but they offer a unified treatment of both reaction rate and regiochemistry, in both type I and type II 1,3-dipoles.

Actually, the qualitative distinction between DZM (a classical type I 1,3-dipole) and DZA (a classical type II 1,3-dipole[10c]) tends to disappear because, even in DZM, the interactions where the dipole acts as an acceptor are found to be necessary. For a quantitative appreciation, the percentages of the contribution of DP (donor) ⟶ DF (acceptor) interactions over the total CT energy are reported in Table 5.

According to these results, DZA acts less as a donor than DZM, but its donor contribution is very high, even with enamines; in DZM cycloadditions, on the other hand, the contribution of the interactions, where the 1,3-dipole acts as an acceptor is larger than expected for its reputation as a donor, at least with strong acceptors.[35]

In conclusion, the results discussed show that only at the level of total charge-transfer energy both the aspects of diazoalkane cycloaddition are reconciled with the experimental findings; moreover, the analysis of the role of groups of interactions, allows one to recover the chemical meaning in the calculations.

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21. Some of the regiochemical results were controlled; in particular we confirmed that DZM reacts with phenyl vinyl sulphone to give only the regioisomer A and with trans-methyl styryl sulphone and trans-phenyl styryl sulphone to yield mixtures of adducts (A:B=25:75 and 40:60, respectively, by ^{1}HNMR analysis of the crude reaction mixtures); trans-methyl propenyl sulphone yielded A, in agreement with the results previously reported for trans-n-dodecyl propenyl sulphone.[17] Careful TLC and NMR analysis of the reaction between DZA and styrene, under different conditions (solvent, temperature, added bases) allowed us to rule out the formation of detectable amounts of adduct B. The cycloaddition of DZA with excess n-butyl vinyl ether at 95°C gave rise to a mixture of products. One of the dominant products results from the reaction of two DZA molecules for each dipolarophile molecule. The structure of these compounds is under investigation. Full results will be published in due time.
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28. Significantly, the various dipolarophiles require different energies to reach equivalent distortions; distortion energy (E_{dis} kJmol^{-1}, CNDO/2) is linearly correlated to log k_2 (e.g. for α=30° log k_2= -0.18 E_{dis} + 24.13, n=8, r=0.88 for DZM): the result is quite reasonable (notice that low distortion energies correspond to high rate constants) and conforms to recent conclusions of ours[13] about the comparison of syn and anti deformations in cis-disubstituted cyclobutenes to explain anti/syn stereoselectivity of DZM cycloaddition. Although deserving investigation, distortion energy cannot distinguish between regioisomers (the correlation itself exists only because the n reactions considered give the same type of adduct); this finding is, for now, a by-product of our study.
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35. A similar conclusion was reached by Huisgen (Ref. 1, vol. 1, pages 132-135) on the basis of frontier interaction energies.