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A Theoretical Evaluation of the Michael-Acceptor Ability of Conjugated Nitroalkenes

Vishal Rai[a] and Irishi N. N. Namboothiri*[a]

Dedicated to Prof. K. Venkatesan on the occasion of his 75th birthday

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A theoretical evaluation of the relative Michael-acceptor abilities of a variety of substituted aromatic and aliphatic nitroalkenes is reported. Several global and local reactivity indices were evaluated with the incorporation of natural charge obtained from natural bond orbital (NBO) analysis. Natural charges at the carbon atom β to the NO_2 group and the condensed Fukui functions derived by this method were quite consistent with the reactivity. The reactivity of nitroalkenes was further examined by kinetic experiments that were monitored by NMR spectroscopy. The isolated yields reported in the literature were also found to have a dependable correlation with these reactivity indices in the majority of cases. The computational methods employed in the calculation of natural charge, the condensed Fukui function, local softness and other reactivity parameters were chosen after evaluation of various methods for their ability to satisfactorily predict the NMR chemical shift of the ^1H atom β and *cis* to the NO_2 group (β-H) in nitroalkenes. Our approach appears suitable for predicting the relative Michael-acceptor abilities of various nitroalkenes, based on the β-carbon natural charge and the indices derived from it.

Introduction

Conjugated nitroalkenes are valuable precursors to a wide variety of intermediates and targets in organic synthesis by virtue of their ability to react as dienophiles, heterodienes, 1,3-dipoles and, above all, as Michael acceptors.[1] Conjugate addition of carbon and heteroatom nucleophiles to nitroalkenes represents the initiating step not only for introducing substituents by enolate trapping, but also for other useful synthetic transformations including those involving the NO_2 group.[1,2] This is primarily because of the unique umpolung reactivity of the nitroalkyl moiety and its ability to undergo facile conversion to functionalities such as 1,3-dipoles, alkyl radicals, carbonyl groups, and oximes.[2] Furthermore, ring-closing reactions initiated by the Michael addition to nitroalkenes provide functionalized and fused rings, often with high stereoselectivity, in a single step. While the NO_2 group in the 1,4-adduct is a "silent spectator" in some ring-closing reactions,[3] other such reactions involve the NO_2 group directly.[4,5] Recent successes in the catalytic[6] and other[7] approaches to the asymmetric version of conjugate addition to nitroalkenes[8] re-emphasize the pivotal role nitroalkenes play as powerful Michael acceptors in the synthesis of complex molecular frameworks, including numerous functionalized ring systems, especially heterocycles.

Despite their well-documented Michael-acceptor ability, nitroalkenes sometimes behave abnormally, for instance, in their reaction with organometallic reagents[9] and as substrates in the Morita–Baylis–Hillman (MBH) reaction,[10,11] to mention a few. A multitude of reasons have been suggested to explain these abnormalities such as single electron transfer, oligomerization/polymerization, attack of the reagents on the primarily formed nitronates, multiple additions, and reversibility in the conjugate additions, some of which are attributable to the nature of the substrate substituents.[9,11] Therefore, the reactivity of nitroalkenes, especially as Michael acceptors, is still speculative. Furthermore, appreciable differences have been observed experimentally in the reactivity of aliphatic and aromatic (including heteroaromatic) nitroalkenes and in their sensitivity to remote substituents (e.g. substituents on the aromatic ring of β-nitrostyrene). Kinetic studies performed by Bernasconi and co-workers on the addition of piperidine and morpholine to a series of β-nitrostyrenes in water and DMSO/water suggested an energetic advantage of having the negative

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[a] Department of Chemistry, Indian Institute of Technology, Bombay,
Mumbai 400076, India
Fax: +91-22-2576-7152
E-mail: irishi@iitb.ac.in

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charge delocalized into the NO_2 group in the transition state.[12] A radical anionic character for the transition state (vide infra) was proposed by Hoz and Gross through their kinetic studies on the addition of cyanide to a series of 1,1-diarylnitroethylenes in water and DMSO.[13] More recently, the kinetics of the addition of thiophenol to *para*-substituted β-nitrostyrenes in acetonitrile/water showed an acceleration of the reaction rate by electron-withdrawing substituents.[14] All three groups observed a Hammett-type correlation of the reactivity with the substituents, which was also influenced by the nature of the solvent.[12–14]

Recently, Mondal et al. investigated the reactivity of various α,β-unsaturated carbonyl compounds towards nucleophiles by the local hard-soft acid-base (HSAB) approach.[15] This study indicated the suitability of employing local reactivity indices such as local softness and the Fukui function for describing the activation of the C=C bond towards nucleophilic attack. In a related work, Domingo et al. described the reactivity of a variety of activated alkenes, including some nitroalkenes, by global and local electrophilicity indices and tested the ability of their model to predict the reactivity of certain Michael acceptors.[16] However, in view of the intriguing reactivity of nitroalkenes owing to strong electron delocalization, the development and experimental evaluation of a methodology for the prediction of the Michael-acceptor ability of nitroalkenes appeared desirable. Therefore, we report here our results on the correlation of the reactivity of nitroalkenes as Michael acceptors with the nature of substituents through the application of ab initio and hybrid density functional theoretical (DFT) methods, which were selected on the basis of NMR analysis. The results are interpreted with the help of natural bond orbital (NBO) analysis, a method which has been successfully applied to localized and delocalized systems in many cases.[17] To the best of our knowledge, the application of the NBO method of analysis for the interpretation of the substituent effects on the reactivity of substrates also appears novel.

Theoretical Background

Electron density is sensitive to structural perturbations and responds to changes in external conditions, and its sensitivity and responsiveness were found to be more important than its absolute value in reflecting the chemical reactivity of a system. This also led to the development and application of reactivity indices derived from electron density.[18] Many well-known chemical concepts such as chemical potential (μ), electronegativity (χ), hardness (η), and softness (S) naturally appear within the framework of DFT.[19] In a more localized approach, these parameters may also emerge as a useful tool for rationalizing, interpreting and predicting the diverse aspects of chemical bonding, reactivity and reaction mechanism. The theoretical research efforts in this area in the past years have made it possible to provide more details about local applications of both ab initio SCF and DFT calculations.[20] The mathematical expression and application of these quantities have been well presented.[21] However, there are only a few reports, to the best of our knowledge, where these parameters have been applied to understand conjugate-addition chemistry.[22] The electronic distribution cannot be directly determined, but it reveals itself in several chemical phenomena that can be experimentally explored to obtain its measure. Several methods based on magnetic properties are used to probe the magnetic shielding at a given point in space.[23] The NMR chemical shifts of protons and other nuclei can be conveniently used to not only explore the extent of π-conjugation but also to gain insight into the electronic environment at an atom of interest.

Chemical potential (μ), electronegativity (χ), hardness (η), and softness (S) are defined as follows[24] (E, N, and V are energy, number of electrons, and external potential of the system, respectively) [Equation (1)]:

$$\chi = -\mu = -\delta E/\delta N_{|V};\ 2\eta = 1/S = -\delta^2 E/\Delta N^2{}_{|V} = -\delta\mu/\delta N_{|V} \qquad (1)$$

These interrelated global parameters have found wide applicability, where a high value of μ and low value of η can characterize a good electrophile. On the other hand, the maximum amount of electronic charge that an electrophilic system can accept is given by, ΔN_{max} ($= -\mu/\eta$). Parr et al. have also proposed the electrophilicity index as, ω ($= \mu^2/2\eta$).[25] In order to understand the reactivity of nitroalkenes, where regioselectivity is well established, these parameters can be utilized, preferably in a localized approach. Local softness ($s^+{}_{\beta\text{-C}}$) and the Fukui function ($f^+{}_{\beta\text{-C}}$) are mutually related, as in Equation (2):[26]

$$f^+{}_{\beta\text{-C}} = \delta\rho/\delta N_{|V} = \delta\mu/\Delta V_{|N};\ s^+{}_{\beta\text{-C}} = f^+{}_{\beta\text{-C}}\cdot S \qquad (2)$$

In a way, the Fukui function represents the response of the chemical potential of a system to a change in external potential. There are several systems for which it has been shown, through ab initio calculations, that a soft electrophile prefers the site with the maximum Fukui function.[27] In finite difference approximation, the condensed Fukui function for the β-C atom (with β-carbon electron density, β-CED) within a molecule gives an expression for nucleophilic attack, as in Equation (3):

$$f^+{}_{\beta\text{-C}} = [q_{\beta\text{-C}}(N+1) - q_{\beta\text{-C}}(N)] \qquad (3)$$

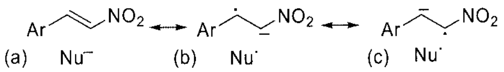
The electrophilicity index (ω or ΔN_{max}) may be defined further in its local form as, $\omega^+{}_{\beta\text{-C}}$ ($= \omega f^+{}_{\beta\text{-C}}$) or $\Delta N_{max}{}^+{}_{\beta\text{-C}}$ ($= \Delta N_{max} f^+{}_{\beta\text{-C}}$).[28] These have been utilized to obtain the electrophilicity patterns of carbenes,[29] cations,[30] and active sites in Diels–Alder reactions.[31]

Natural atomic orbitals (NAOs) are localized one-center effective natural orbitals of an atom in the molecular environment. The distinguishing feature of NAOs is their spatial diffuseness, which is optimized for effective atomic charge and the incorporation of important nodal features due to steric confinement. Thus, NAOs account for realistic local charge shifts and steric properties in the molecular environment. This clearly gives NAOs an edge over isolated atom natural orbitals and standard basis orbitals. Hence, NAOs are defined as eigen orbitals of the density operator for an atom. Parallel to the one-center NAOs, the natural bond orbitals (NBOs) can be described as local two-center eigen vectors of the density operator, preserving the maximum occupancy, orthonormality, and integrity properties of natural orbitals. NBOs may have limited practical value in highly delocalized systems, as they are strictly localized. Therefore, a semi-localized alternative [the natural localized molecular orbital (NLMO)] is used, which closely resembles the parent NBO and also captures the associated delocalizations. NLMOs adopt the characteristic bonding pattern of a localized Lewis structure, averting symmetry imposed-mixing that limits the transferability and interpretability of canonical molecular orbitals.[17]

Applying the above facts, we analyzed nitroalkenes in terms of localized electron pair bonding units. The program employed carries out the determination of NAOs, natural hybrid orbitals, NBOs and NLMOs and uses these to perform natural population analysis (NPA). This approach is not based on a unitary transformation of the occupied MOs, as in previous methods, but on a mixing of the occupied and virtual spaces that localize bonds and lone pairs as basic units of the molecular structure. We derived the β-CED of nitroalkenes from NPA, which was further used to calculate the condensed Fukui function ($f^{+}_{\beta\text{-C}}$) and local softness ($s^{+}_{\beta\text{-C}}$). The Fukui function may also be considered as a normalized local softness. Therefore, the reactivity indices, namely β-CED and $f^{+}_{\beta\text{-C}}$, have been used in parallel to explain the reactivity of various nitroalkenes. This approach may simplify the understanding of the reactivity of various Michael acceptors.

Results and Discussion

The parameters derived from basic properties of nitroalkenes governed by small changes away from the initial state are of great importance. In the Michael addition to nitroalkenes, the transition state is not an intermediate structure between that of the reactant and the product. It was proposed and experimentally confirmed to have a partial radical character along with partial charge.[32] Therefore, further transfer of spin density from the nucleophile to a nitroalkene should take place on the resonating structures thus formed (Scheme 1). The relative contribution of these structures to the transition state structure is governed by intrinsic parameters such as the activating group and the solvent, but the final outcome will probably depend largely on the relative contribution of the structure having a radicaloid center at the benzylic carbon [Scheme 1 (b)]. This, in turn, will depend on the activating group, the substituents, and the coplanarity of the substrate. However, it is clear that substituents with a positive mesomeric effect will be very effective in stabilizing the radical center at the benzylic carbon atom [Scheme 1 (b)], leading to the high reactivity of nitroalkenes with electron-donating substituents. It is obvious that the precise situation in a given case demands its own detailed examination, but our parameters are expected to have a significant contribution in most cases. The β-CED explains the reactivity of nitroalkenes on the basis of neutral resonance structure (a) [Scheme 1 (a)], whereas the condensed Fukui function [Equation (3)] considers both neutral and radicaloid structures (b) and (c) [Scheme 1 (b), (c)]. Since conjugated nitroalkenes have a higher reactivity than most other activated olefins, the ground-state properties should comparatively show more resemblance to that of the transition state with the lowest energy pathway. In other words, the β-CED should be as expressive as $f^{+}_{\beta\text{-C}}$.



Scheme 1. Three major resonance structures (a)–(c) contributing to the transition state.

Electronic delocalization has been investigated by studying the magnetic shielding at a localized point in space by examining NMR chemical shifts (vide supra).[23,33] For the calculation of the chemical shifts of the β-H atom in nitroalkenes **1**–**14** (Figure 1), β-nitrostyrene (**1**) was taken as the benchmark (Table 1). Examination of Table 1 indicates that the B3LYP level of theory with lower basis sets provides chemical shift values for the β-H atom with considerable deviation (ca. 5–10% error, Table 1, Entries 1–4) from the experimental value of δ = 8.011 ppm. However, when a larger basis set [6-311++G(3df, 3pd)] was employed at the B3LYP level, the deviation was minimal (1% error, Table 1, Entry 5). Later, chemical shift values were also calculated at the MP2/6-31G(d) level, which provided comparable results (Table 1, Entry 6).

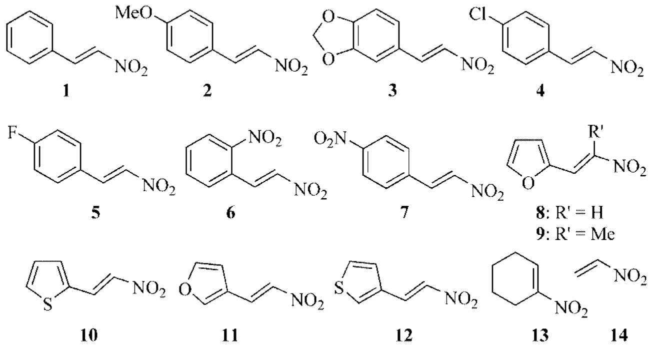


Figure 1. Nitroalkenes chosen for evaluation of reactivity in conjugate additions.

Table 1. Optimization of the level of theory and basis set for estimation of the chemical shift of the proton β and *cis* to the NO_2 group in β-nitrostyrene (**1**).

Entry	Level of theory	Basis set	Calculated δ[a]	% Error[b]
1	B3LYP	6-31G(d)	7.2210	–9.8
2	B3LYP	6-31G(d,p)	7.4903	–6.5
3	B3LYP	6-311G(d,p)	7.5694	–5.5
4	B3LYP	6-311++G(d,p)	7.6230	–4.8
5	B3LYP	6-311++G(3df,3pd)	7.9298	–1.0
6	MP2	6-31G(d)	7.9291	–1.0

[a] All δ values are in ppm. [b] Experimental δ = 8.011 ppm.

The two levels of theory and their corresponding basis sets that were found suitable for the calculation of the chemical shift of the β-H atom were subsequently employed for calculation of the chemical shifts in nitroethylene (**14**, Table 2). Besides the chemical shift of the β-H atom (Table 2, Entry 1), the chemical shifts of the other two protons in nitroethylene (**14**, Table 2, Entries 2 and 3) were also estimated. Overall, both Method A [B3LYP/6-311++G(3df,3pd)//B3LYP/6-31G(d)] and Method B [MP2/6-31G(d)//B3LYP/6-31G(d)] satisfactorily predicted the chemical shift values for H^1, H^2 (β-H) and H^3 (α-H). However, Method B appeared marginally superior to Method A both in terms of the extent of agreement between calculated and experimental values, as well as the requirement of a smaller basis set. Similar trends were found with Method C [MP2/6-31G(d)//B3LYP/6-31+G(d)], as well.

Having confirmed the efficacy of the level of theory used for computing the chemical shifts of the β-H atom in β-nitrostyrene (**1**) and nitroethylene (**14**), the corresponding chemical shifts were calculated in the other nitroalkenes **2**–**13** (Table 3). While Method B appeared superior to Method A for all the aromatic nitroalkenes **1**–**7** and aliphatic nitroalkenes [nitrocyclohexene (**13**) and nitroethylene (**14**)], the converse was true for heteroaromatic nitroalkenes **8**–**12**. This is in terms of the difference between calculated and experimental chemical shifts as expressed in % error. It is important to note that the deviation from the experimental value is <10% in all but two cases (see Table 3, Entries 8 and 9). The chemical shifts with Method C are inferior to those with Methods A and B, but the error is well within acceptable limits. The advantage associated with this method is better consideration of charges during optimiza-

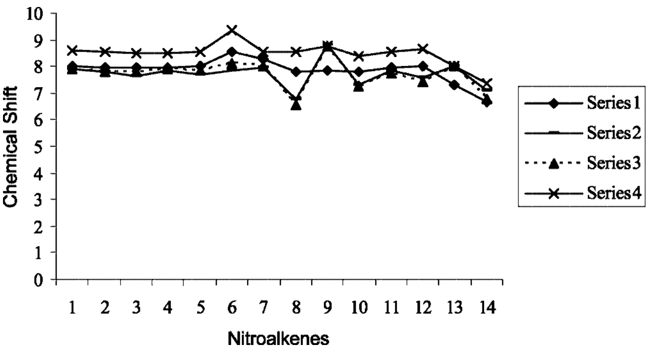
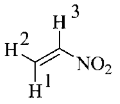


Figure 2. Correlation of theoretical and experimental chemical shift values for the proton β and *cis* to the NO_2 group in nitroalkenes **1**–**14**; Series 1: exp. δ; Series 2: calcd. δ (Method A); Series 3: calcd. δ (Method B); Series 4: calcd. δ (Method C).

Table 2. Calculation of ^{1}H NMR chemical shifts in nitroethylene (**14**).

 Nitroalkene	Entry (H)	Exp. δ	Calcd. δ Method A[a]	% Error Method A[a]	Calcd. δ Method B[b]	% Error Method B[b]	Calcd. δ Method C[c]	% Error Method C[c]
	1	6.6475	7.0906	6.7	6.7700	1.80	7.3865	11.0
	2	5.9540	5.9615	0.8	5.9394	–0.20	6.1902	2.0
	3	7.1625	7.3500	2.6	7.1642	0.02	7.4332	3.8

[a] Method A: B3LYP/6-311++G(3df,3pd)//B3LYP/6-31G(d). [b] Method B: MP2/6-31G(d)//B3LYP/6-31G(d). [c] Method C: MP2/6-31G(d)//B3LYP/6-31+G(d). Method C was employed to take into account the delocalization of an additional electron during the calculation of the condensed Fukui function. The extra diffuse function will lead to small geometry differences, but there are considerable differences in chemical shifts, which is evident in the results. This further emphasizes the importance of NMR validation prior to selection of the analysis method.

Table 3. Calculated ^{1}H NMR chemical shifts of the proton β and *cis* to the NO_2 group in nitroalkenes **1**–**14**.[a]

Entry	Nitroalkene (β, α)	Exp. δ[b]	Theoretical δ[b], % Error Method A[c]	Theoretical δ[b], % Error Method B[d]	Theoretical δ[b], % Error Method C[e]
1	**1** (Ph, H)	8.0110	7.9298, –1.0	7.9291, –1.0	8.5832, 7.1
2	**2** (4-$MeOC_6H_4$, H)	7.9770	7.7811, –2.4	7.8085, –2.1	8.5496, 7.2
3	**3** [3,4-$(OCH_2O)C_6H_3$, H]	7.9310	7.6119, –4.0	7.8223, –1.4	8.4811, 6.9
4	**4** (4-ClC_6H_4, H)	7.9675	7.8561, –1.4	7.8781, –1.1	8.5062, 6.8
5	**5** (4-FC_6H_4, H)	7.9880	7.6748, –3.9	7.8600, –1.6	8.5615, 7.2
6	**6** (2-$O_2NC_6H_4$, H)	8.5410	7.8589, –7.9	8.1113, –5.0	9.3593, 9.6
7	**7** (4-$O_2NC_6H_4$, H)	8.2810	7.9627, –3.8	8.0230, –3.1	8.5549, 3.3
8	**8** (2-furyl, H)	7.7815	6.7808, –12.9	6.5612, –15.7	8.5336, 9.7
9	**9** (2-furyl, Me)	7.8600	8.7920, 11.9	8.7834, 11.7	8.7656, 11.5
10	**10** (2-thienyl, H)	7.7700	7.3001, –6.0	7.2585, –6.6	8.3903, 7.9
11	**11** (3-furyl, H)	7.9410	7.8415, –1.3	7.7319, –2.6	8.5409, 7.6
12	**12** (3-thienyl, H)	8.0165	7.5876, –5.4	7.4393, –7.2	8.6394, 7.8
13	**13** [-$(CH_2)_4$-]	7.3250	7.9895, 9.0	8.0295, 8.8	8.0120, 9.4
14	**14** (H, H)	6.6475	7.0906, 6.2	6.7700, 1.8	7.3865, 11

[a] SCF GIAO (self consistent field guage including atomic orbital) magnetic shielding tensors have been taken for predicting NMR values in all cases, as SCF magnetic shielding tensors were found to be more realistic in comparison to MP2 magnetic shielding tensors. SCF density was taken for NBO analysis. [b] All chemical shift (δ) values are in ppm. [c] Method A: B3LYP/6-311++G(3df,3pd)//B3LYP/6-31G(d). [d] Method B: MP2/6-31G(d)//B3LYP/6-31G(d). [e] Method C: MP2/6-31G(d)//B3LYP/6-31+G(d).

tion of nitroalkenes with $N + 1$ electrons. The extent of agreement between the calculated and the experimental chemical shifts is delineated in Figure 2.

NBO Analysis of Charge Density Distribution

The β-CED and the corresponding electron density at the α-carbon atom (α-CED) of nitroalkenes **1**–**14** were calculated at the MP2/6-31G(d) level of theory (Table 4). From comparison of the β-CED and α-CED in nitroalkenes **1**–**14**, it is obvious that nitroalkenes **7**, **8**, **9**, **13**, and **14** have a higher electron density at the β-C atom than at the α-C atom. While this result can be attributed to the negative mesomeric (–M) and negative inductive (–I) effects of the NO_2 group for **7**, to the –I effect of the furyl oxygen atom for **8**, and to the –I effect of the furyl oxygen atom in conjunction with the positive inductive (+I) and hyperconjugative effects of the α-Me group for **9**,[34] the scenario appears fundamentally different for **13** and **14**. In aromatic nitroalkenes **1**–**6** and heteroaromatic nitroalkenes **10**–**12**, β-CED < α-CED, indicating the predominance of the powerful electron-withdrawing nature of the NO_2 group. Alternatively, the aromatic ring, in the absence of a suitably placed strongly electron-withdrawing group, donates electrons to the nitroethylenic moiety, causing polarization of the double bond towards the NO_2 group. In the absence of such an aromatic ring β to the NO_2 group, β-CED > α-CED, as in **13** and **14**.[35]

Table 4. β-CED and α-CED for nitroalkenes **1**–**14**, as calculated by NPA.

Entry	Nitroalkene (β, α)	Natural charge Method B[a]		Natural charge Method C[b]	
		β-C	α-C	β-C	α-C
1	**1** (Ph, H)	–0.1013	0.1389	–0.0997	0.1391
2	**2** (4-MeOC_6H_4, H)	–0.0904	0.1548	–0.0883	0.1553
3	**3** [$3,4\text{-}(OCH_2O)C_6H_3$, H]	–0.0983	0.1441	–0.0965	0.1443
4	**4** (4-ClC_6H_4, H)	–0.1077	0.1323	–0.1060	0.1326
5	**5** (4-FC_6H_4, H)	–0.1018	0.1405	–0.1005	0.1403
6	**6** ($2\text{-}O_2NC_6H_4$, H)	–0.1136	0.1240	–0.1121	0.1241
7	**7** ($4\text{-}O_2NC_6H_4$, H)	–0.1283	0.1072	–0.1273	0.1072
8	**8** (2-furyl, H)	–0.1485	0.1352	–0.1469	0.1354
9	**9** (2-furyl, Me)	–0.1679	0.0749	–0.1670	0.0749
10	**10** (2-thienyl, H)	–0.1264	0.1330	–0.1242	0.1337
11	**11** (3-furyl, H)	–0.1008	0.1460	–0.0990	0.1465
12	**12** (3-thienyl, H)	–0.1003	0.1418	–0.0988	0.1423
13	**13** [$-(CH_2)_4-$]	–0.1053	0.0475	–0.1046	0.0477
14	**14** (H, H)	–0.3111	0.1343	–0.3109	0.1341

[a] Method B: MP2/6-31G(d)//B3LYP/6-31G(d). [b] Method C: MP2/6-31G(d)//B3LYP/6-31+G(d); method A also showed a similar trend. Smaller differences of charges in a few cases made it necessary to further evaluate these systems with other parameters.

The β-CED, apart from being much more consistent than charge densities derived from other methods, was found to have less dependence on a basis set with an additional diffuse function used during optimization (Figure 3). This suggests that the β-CED is a dependable electrophilicity index.

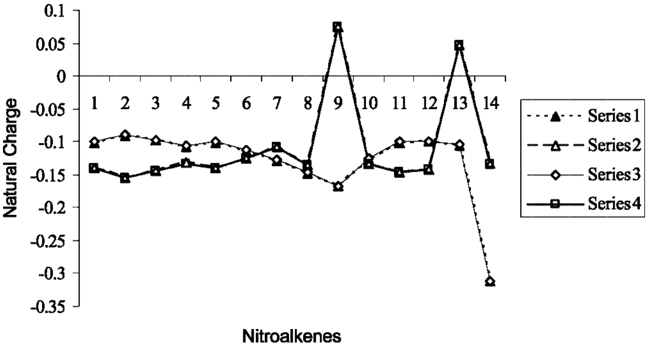


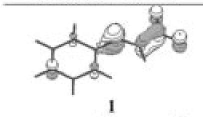
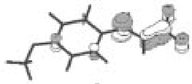
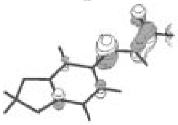
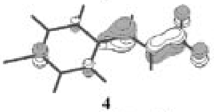
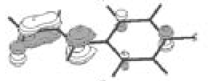
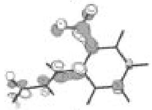
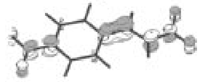
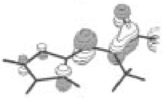
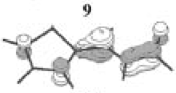
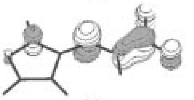
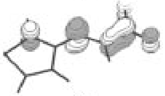
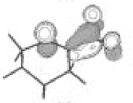
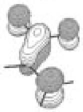
Figure 3. Distribution of charge at the β- and α-C atoms in nitroalkenes **1**–**14**. Series 1 and 2: electron density at the β- and α-C atoms, respectively, with Method B: MP2/6-31G(d)//B3LYP/6-31G(d); Series 3 and 4: electron density at the β- and α-C atoms, respectively, with Method C: MP2/6-31G(d)//B3LYP/6-31+G(d); overlapping of Series 1 & 3 and Series 2 & 4 shows the reliability of the β-CED and α-CED as calculated by the applied methods.

The β-CED was calculated at various higher levels of theory to verify the accuracy and consistency of this parameter (Table S2, Supporting Information). The magnitude of parameter varies when the density is taken from different methods but the consistency is maintained throughout the method used as is obvious from Figure S1 (Supporting Information), which ensures the adequacy of the method.

After Parr's contribution in the past decade, various quantities representing the response of a system's energy to perturbation in its number of electrons and external potential were revealed. The chemical hardness (η), proposed by Parr and Pearson, represents the resistance of a system to changes in its number of electrons.[36] The chemical softness (S) is naturally defined as the inverse of η. In other words, hardness is a measure of stability and softness is a measure of reactivity. While the global properties may explain the reactivity of nitroalkenes, for understanding the conjugate addition to nitroalkenes, we focused more on local parameters. $\Delta N_{\max}{}^{+}{}_{\beta\text{-C}}$ and $\omega^{+}{}_{\beta\text{-C}}$ were found to be in low to moderate accordance with expected behavior (Table S2 and Figure S1, Supporting Information).

The most important local quantity in the case of nitroalkenes is the electron density itself (β-CED). Chemical reactions are mainly the adjustment of valence electrons among the reactant orbitals. Fukui proposed his frontier molecular orbital theory (FMO), which allows a chemical reaction to be understood in terms of the HOMO and LUMO.[37] Fukui functions are based on this concept, whereas condensed Fukui functions at the β-C atom in a molecule can be defined in terms of associated electron populations. The largest value of $f^{+}{}_{\beta\text{-C}}$ at the reaction site will be preferable, as it implies a large difference in chemical potentials. Since the soft species are large in size with a small charge, it is expected that in soft–soft reactions covalent bonding will predominate. The nuclear charge is adequately screened by the core electrons, and the two soft species mainly interact through frontier orbitals. Energy changes due to covalent interactions (ΔE_{cov}) dominate electrostatic and polarization factors in the case of soft–soft interactions, where minimi-

Table 5. Local reactivity indices.

Nitroalkene LUMO[a]	$\lvert f^{+}_{\beta\text{-C}}\rvert$[b]	$\lvert f^{+}_{\beta\text{-C}}\rvert$[c]	$\lvert s^{+}_{\beta\text{-C}}\rvert$[b]	$\lvert s^{+}_{\beta\text{-C}}\rvert$[c]	β-CED[b]	β-CED[c]
 **1**	0.1592	0.1587	0.4290	0.4270	–0.1013	–0.0997
 **2**	0.1698	0.1700	0.4759	0.4772	–0.0904	–0.0883
 **3**	0.1638	0.1634	0.4680	0.4678	–0.0983	–0.0965
 **4**	0.1538	0. 1535	0.4201	0.4205	–0.1077	–0.1060
 **5**	0.1597	0.1591	0.4298	0.4285	–0.1018	–0.1005
 **6**	0.0145	0.0536	0.0377	0.1389	–0.1136	–0.1121
 **7**	0.1362	0.0851	0.3723	0.2332	–0.1283	–0.1273
 **8**	0.1867	0.1545	0.5282	0.4385	–0.1485	–0.1469
 **9**	0.1278	0.1275	0.3618	0.3619	–0.1679	–0.1670
 **10**	0.1513	0.1508	0.4269	0.4270	–0.1264	–0.1242
 **11**	0.1665	0.1662	0.4383	0.4387	–0.1008	–0.0990
 **12**	0.1616	0.1610	0.4295	0.4292	–0.1003	–0.0988
 **13**	0.1551	0.1543	0.3423	0.3409	–0.1053	–0.1046
 **14**	0.1676	0.1670	0.3452	0.3446	–0.3111	–0.3109

[a] Contours have been plotted with a contour value of 0.08, derived from FMO calculations with Method C: MP2/6-31G(d)//B3LYP/6-31+G(d). [b] Parameters calculated with Method B: MP2/6-31G(d)//B3LYP/6-31G(d); all values of $f^{+}_{\beta\text{-C}}$ and $s^{+}_{\beta\text{-C}}$ are negative. [c] Parameters calculated with Method C: MP2/6-31G(d)//B3LYP/6-31+G(d); all values of $f^{+}_{\beta\text{-C}}$ and $s^{+}_{\beta\text{-C}}$ are negative.

zation of ΔE_{cov} leads to the HSAB principle.[27] A local version of the HSAB principle ($s^{+}_{\beta\text{-C}}$) has also been derived with this approach. The amount of electronic charge transferred between the reactants during soft–soft interactions (which are covalent, and hence, controlled by frontier orbitals during the small displacement along the reaction coordinate) is large for small values of η with maximum overlap of the Fukui functions and larger values of $f^{+}_{\beta\text{-C}}$ (or equivalently, local softness, $s^{+}_{\beta\text{-C}}$). Michael addition to nitroalkenes mainly involves interaction of the nitroalkene LUMO with the nucleophile HOMO. The character of the LUMO is an important controller of reactivity, as it is the virtual orbital that captures an external electron to form an anion. The LUMOs of nitroalkenes are given in Table 5, which shows the delocalization of orbitals due to the presence of highly conjugated π-systems. Also, we can see that the predominant contribution to the LUMO is from the β-C atom.

The earlier reports utilized Mulliken population analysis (MPA) for deriving various reactivity parameters.[20,22] Comparative analysis of β-CED and MPA-derived local parameters show that the β-CED from both methods are broadly consistent with each other, but MPA provides erroneous results in a few cases. Further comparison of condensed Fukui functions shows large differences, as expected, due to the involvement of radical anions, thus displaying the shortcomings of MPA. The abnormal values in the case of the β-CED of nitroalkenes **6** and **10** and $f^{+}_{\beta\text{-C}}$

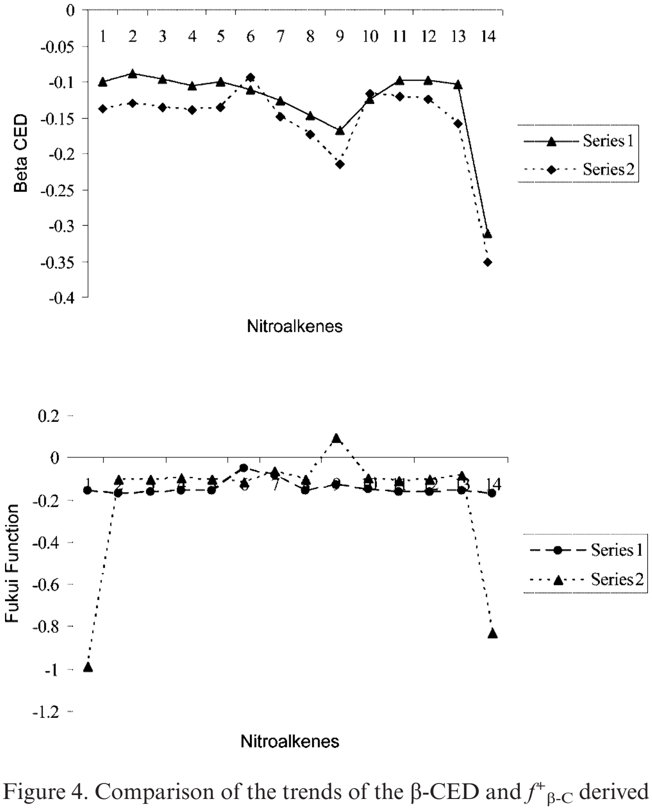


Figure 4. Comparison of the trends of the β-CED and $f^{+}_{\beta\text{-C}}$ derived by natural and Mulliken charges. Series 1: natural charge derived β-CED and $f^{+}_{\beta\text{-C}}$, respectively; Series 2: MPA derived β-CED and $f^{+}_{\beta\text{-C}}$, respectively.

Table 6. Local reactivity indices (NBO vs. MPA).

Entry	Nitroalkene (β, α)	$\lvert f^{+}_{\beta\text{-C}}\rvert$[a]	$\lvert f^{+}_{\beta\text{-C}}\rvert$[b]	$\lvert s^{+}_{\beta\text{-C}}\rvert$[a]	$\lvert s^{+}_{\beta\text{-C}}\rvert$[b]	β-CED[a]	β-CED[b]
1	**1** (Ph, H)	0.1587	0.9918	0.4270	2.6683	–0.0997	–0.1379
2	**2** (4-MeOC_6H_4, H)	0.1700	0.1056	0.4772	0.2968	–0.0883	–0.1302
3	**3** [3,4-(OCH_2O)C_6H_3, H]	0.1634	0.1015	0.4678	0.2907	–0.0965	–0.1359
4	**4** (4-ClC_6H_4, H)	0.1535	0.0974	0.4205	0.2667	–0.1060	–0.1389
5	**5** (4-FC_6H_4, H)	0.1591	0.1005	0.4285	0.2705	–0.1005	–0.1356
6	**6** (2-$O_2NC_6H_4$, H)	0.0536	0.1182	0.1389	0.3064	–0.1121	–0.0937
7	**7** (4-$O_2NC_6H_4$, H)	0.0852	0.0658	0.2332	0.1801	–0.1273	–0.1494
8	**8** (2-furyl, H)	0.1545	0.1010	0.4385	0.2866	–0.1469	–0.1732
9	**9** (2-furyl, Me)	0.1275	0.0935	0.3619	0.2654	–0.1670	–0.2157
10	**10** (2-thienyl, H)	0.1508	0.0941	0.4270	0.2666	–0.1242	–0.1171
11	**11** (3-furyl, H)	0.1662	0.1072	0.4387	0.2829	–0.0990	–0.1203
12	**12** (3-thienyl, H)	0.1610	0.1023	0.4292	0.2729	–0.0988	–0.1252
13	**13** [-$(CH_2)_4$-]	0.1543	0.0856	0.3409	0.1891	–0.1046	–0.1581
14	**14** (H, H)	0.1670	0.8270	0.3446	1.7065	–0.3109	–0.3507

[a] NBO-derived parameters with Method C: MP2/6-31G(d)//B3LYP/6-31+G(d); all values of $f^{+}_{\beta\text{-C}}$ and $s^{+}_{\beta\text{-C}}$ are negative. [b] MPA-derived parameters with Method C: MP2/6-31G(d)//B3LYP/6-31+G(d); all values of $f^{+}_{\beta\text{-C}}$ and $s^{+}_{\beta\text{-C}}$ are negative.

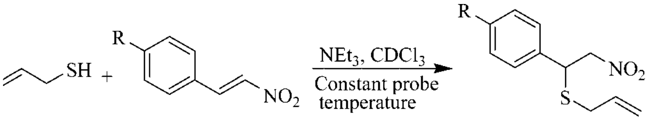
for several nitroalkenes such as **1**, **6**, **9**, and **14** show the inconsistent behavior of MPA-derived charge densities (Table 6, Figure 4).

Substituent Effect on the Reactivity of Nitroalkenes as Michael Acceptors – Correlation of Experimental Results with Electrophilicity Indices

Prior to making any attempt to correlate the experimental results available in the literature (Supporting Information) on the Michael addition of various nucleophiles to nitroalkenes with our electrophilicity indices, we performed model experiments to compare reactivity parameters with the reaction kinetics. This is because the reaction time and the conditions of the reported reactions might vary considerably in many cases, making a meaningful correlation of the electrophilicity indices with the reactivity of nitroalkenes (expressed in isolated yields of the Michael adducts) extremely challenging. Secondly, the kinetic data available in the literature for the conjugate addition of amines, cyanide and thiophenol to nitroalkenes, were based on reactions carried out in water, water/DMSO or water/acetonitrile mixtures.[12–14]

In view of the concerns outlined above, we examined the reactivity of representative nitroalkenes **1**, **2**, and **7** with the nucleophile 2-propene-1-thiol (**15**) in a non-interacting solvent ($CDCl_3$) by performing kinetic experiments using ^{1}H NMR spectroscopy (Table 7).[38] When the reaction was carried out at 25 °C with a nitroalkene/2-propene-1-thiol ratio of 2:1 and analyzed after 2 min, 100% conversion was observed for *p*-methoxy-β-nitrostyrene (**2**), but only 98% and 91% conversion were observed for β-nitrostyrene (**1**) and *p*,β-dinitrostyrene (**7**), respectively (Table 7, Entries 1–3, Exp. 1). When the reaction mixture was analyzed after 5 min, the conversion of β-nitrostyrene (**1**) was also complete. However, *p*,β-dinitrostyrene (**7**) was the least reactive, with only 94% conversion observed after 5 min. Although this experiment suggested that nitroalkene **7** is the least reactive among the three, and nitroalkene **2** is marginally more reactive than **1**, under the conditions employed, an independent verification was sought to confirm this observation. Therefore, in a separate experiment, the reaction was performed at a lower temperature (18.6 °C) and with a nitroalkene/2-propene-1-thiol ratio of 1:1 (Table 7, Exp. 2). Analysis of the reaction mixture after 4 min showed that while nitroalkene **2** underwent 71% conversion, **1** underwent only 69% conversion, and **7** was much less reactive (57% conversion), as in the previous experiment (Table 7, Entries 1–3, Exp. 2). These studies confirmed the reactivity order in *p*-substituted nitrostyrenes **1**, **2** and **7** as *p*-methoxy-β-nitrostyrene > β-nitrostyrene > *p*,β-dinitrostyrene and is consistent with the reactivity indices derived from high-level theoretical calculations.

Table 7. Kinetics of Michael addition of 2-propene-1-thiol (**15**) to nitroalkenes **1**, **2** and **7**.



15 **1**: R = H; **2**: OMe; **7**: NO_2 **16a–c**

Entry	Nitroalkene (β, α)	β-CED[a]	$\lvert f^{+}_{\beta\text{-C}}\rvert$[a]	Exp. 1 % Conversion at 25 °C[b] 2 min	Exp. 1 % Conversion at 25 °C[b] 5 min	Exp. 2 % Conversion at 18.6 °C[c] 4 min
1	**1** (Ph, H)	–0.0997	0.1587	98	100	69
2	**2** (4-MeOC_6H_4, H)	–0.0883	0.1700	100	100	71
3	**7** (4-$O_2NC_6H_4$, H)	–0.1273	0.0851	91	94	57

[a] Reactivity indices were derived by MP2/6-31G(d)//B3LYP/6-31+G(d), see Tables 4 and 5. [b] A nitroalkene/2-propene-1-thiol ratio of 2:1 was used; % conversions with respect to 2-propene-1-thiol were determined by ^{1}H NMR spectroscopy. [c] A nitroalkene/2-propene-1-thiol ratio of 1:1 was used; % conversions with respect to 2-propene-1-thiol were determined by ^{1}H NMR spectroscopy.

The above observation confirmed the fact that the electrophilicity indices, the β-CED and condensed Fukui function, explain the reactivity of nitroalkenes in non-interacting solvents with good reliability. The self-consistent reaction field polarized continuum model was used to examine the nature of nitroalkenes in the solvent (chloroform) in which the kinetic experiments were carried out (Table S8, Supporting Information). The results were found to be consistent with those obtained from gas-phase calculations. Interestingly, we found that the β-CED for *p*-methoxy-β-nitrostyrene (**2**) is less than that of *p*,β-dinitrostyrene (**7**) in the ground state [Scheme 1 (a)], but the trend reverses after the addition of an electron to the system. Thus, the relative contribution of the ground-state structure [Scheme 1 (a)] should be more than that of the radical anions [Scheme 1 (b)–(c)]. This fact again supports the consistency of the β-CED with $|f^{+}_{\beta\text{-C}}|$, which considers the contributions from all three structures [Scheme 1 (a)–(c)]. However, if radical anions are stabilized by an interacting solvent or other medium, leading to a higher contribution towards the transition state, the reactivity trend will be defined by their β-CED.

Our kinetic studies confirmed the suitability of our calculation results on the extent of polarizability of the double bond in conjugation with the aryl ring and the NO_2 group in the form of local softness ($s^{+}_{\beta\text{-C}}$) and, more importantly, the β-CED and condensed Fukui function ($f^{+}_{\beta\text{-C}}$). Additionally, our calculation methods reliably predicted the Michael-acceptor ability of conjugated nitroalkenes. We then decided to evaluate some of the experimental results available in the literature on the Michael-type addition of various carbon- and heteroatom-centered nucleophiles to conjugated nitroalkenes. The representative examples chosen from the literature involve reactions of nitroalkenes with heteroatom nucleophiles (2-aminobenzaldehyde),[39] *C*-centered nucleophiles (indole and malonate),[40,41] and an organometallic reagent (Fischer aminocarbene complex).[42] Our analysis has shown that the parameters discussed above [local softness ($s^{+}_{\beta\text{-C}}$), the β-CED and Fukui function ($f^{+}_{\beta\text{-C}}$)] correlate well with the isolated yields in a majority of the cases and moderately well with the reaction time (see Supporting Information for further discussion). Thus, these parameters might serve as a useful tool for analyzing the reactivity of nitroalkenes with other Michael donors. The methodology may find further applications towards better understanding the reactivity of other Michael acceptors.

Conclusions

The Michael-acceptor ability of a variety of substituted aromatic and aliphatic conjugated nitroalkenes was analyzed by correlating the condensed Fukui function and the β-CED with the rate of reaction of the nitroalkenes and the % conversion or isolated yields of the 1,4-adducts. Kinetic studies carried out in a non-interacting solvent showed that the reactivity indices are indeed reliable. Further correlation with the experimental results available in the literature on the conjugate addition of a variety of carbon and heteroatom nucleophiles to nitroalkenes has shown the efficacy of these parameters in explaining the observed reactivity. The isolated yields showed excellent agreement with the condensed Fukui function and β-CED derived from NBO analysis, but FMO condensed parameters such as local softness (*S*) and electrophilicity indices ω and $\Delta N_{\max}$ were not general with either MPA or NBO analysis derived charge densities. Calculations of the condensed Fukui function and softness have encountered difficulties earlier, because these required atomic electron population in a molecule which was not unambiguously defined irrespective of the method used. We found that natural charge derived β-CED is a good reactivity index, explaining the reactivity of various nitroalkenes towards conjugate addition on par with the Fukui function. While the electron densities and condensed Fukui functions calculated by the NBO method correlated well with the Michael-acceptor ability of nitroalkenes, the MPA was not suitable. Our studies show that the relative reactivities of conjugated nitroalkenes towards various nucleophiles can be quantified with reasonable accuracy using our table of β-CED and condensed Fukui function values calculated by NBO with the MP2/6-31G(d)//B3LYP/6-31+G(d) method. Extension of the NBO analysis to estimate the behavior of nitroalkenes in reactions other than conjugate additions and to evaluate the reactivity of other activated alkenes appear to be an attractive prospect.

Experimental Section

Computational Methods: All computations were performed with the GAUSSIAN 98, revision A.11.4 program suite[43] with the DFT method of Becke's three-parameter hybrid Hartree–Fock procedure with the Lee–Yang–Parr correlation function (B3LYP) and Møller–Plesset perturbation theory (MP2). The geometries of all the nitroalkenes and their anions in this study were fully optimized by the DFT/B3LYP method with the 6-31G(d) and 6-31+G(d) basis sets. No symmetry constraints were imposed in the optimizations, except for tetramethylsilane (TMS). Split-valence basis sets, polarized basis sets, diffuse functions, and high-angular-momentum basis sets were used to consider highly delocalized molecules. The chemical shifts for the β-H atom in nitroalkenes were calculated by determining the difference of SCF magnetic shielding tensors for TMS and the nitroalkenes (experimental ^{1}H NMR chemical shifts were recorded with TMS as an internal standard). For the purpose of identifying a theoretical method and a basis set suitable for the calculation of the charge density, especially at the β-C atom of conjugated nitroalkenes **1**–**14** (Figure 1), NMR chemical shifts of the β-H atom were calculated at various levels of theory and compared with the experimental chemical shifts (vide infra). ^{1}H was chosen for calculation of the chemical shifts due to its greater sensitivity over ^{13}C, even though its spectral range is modest.[44] The chemical shielding tensors were calculated by the DFT-hybrid GIAO method with TMS as reference. MP2/6-31G(d) and B3LYP/6-311++G(3df,3pd) were found to be practical methods for B3LYP/6-31G(d) as well as B3LYP/6-31+G(d) optimized geometries. Charge densities were calculated by NPA with the NBO 3.1 program, which is included in GAUSSIAN 98, with the strongly delocalized NBO set. MO calculations were performed to give HOMO and LUMO energies with the MP2/6-31G(d)//B3LYP/6-31G(d) method. Contour plots were generated by MOLDEN 4.1. Further calculations were also carried out over B3LYP/6-31+G(d) geometries for proper diffusion and accuracy in Fukui functions. NPA was carried out with the MP2/6-31G(d) and B3LYP/6-311++G(3df,3pd) methods for analyzing the MP2 and SCF density, respectively, with geometries optimized at B3LYP/6-31+G(d), which shows the unchangeability of parameters derived from earlier methods. The electronic chemical potential (μ) and chemical hardness (η) were approximated in terms of the one-electron energies of the FMOs, HOMO and LUMO, ε_H and ε_L, respectively, according to $\mu = (\varepsilon_H + \varepsilon_L)/2$ and $\eta = (\varepsilon_L - \varepsilon_H)/2$, from the valence state parabola model.[45] The ground-state parabola model approximates μ and η as follows: $\mu = (\varepsilon_H + \varepsilon_L)/2$ and $\eta = (\varepsilon_L - \varepsilon_H)$.[25] Global reactivity indices χ, $\Delta N_{\max}$, ω, and S were calculated according to equations mentioned earlier. Local reactivity indices $\omega^{+}_{\beta\text{-C}}$, $\Delta N_{\max}{}^{+}_{\beta\text{-C}}$, $f^{+}_{\beta\text{-C}}$, $s^{+}_{\beta\text{-C}}$, and the β-CED were calculated with charge densities from MPA and NBO analysis (condensed with FMO parameters for $\omega^{+}_{\beta\text{-C}}$, $\Delta N_{\max}{}^{+}_{\beta\text{-C}}$, and $s^{+}_{\beta\text{-C}}$). The self-consistent reaction field polarized continuum model was used to examine the nature of nitroalkenes in a non-interacting solvent system.

Experimental Procedures. Experiment 1: To a solution of nitroalkene **1**, **2**, or **7** (2 mmol) in $CDCl_3$ (3 mL) were added 2-propene-1-thiol (**15**) (0.13 mL, 1 mmol) and Et_3N (0.01 mL, 0.1 mmol). The reaction mixture was stirred at 25 °C. ^{1}H NMR spectra were recorded at the same probe temperature (25 °C) by withdrawing aliquots (0.5 mL each) after 2 and 5 min. The spectra recorded after 2 min showed complete conversion (100%) of **2**, 98% conversion of **1**, and 91% conversion of **7**. After 5 min, the reaction was complete (100% conversion) for nitroalkenes **1** and **2**, but only 94% conversion was observed for **7**. **Experiment 2:** In a separate experiment, to equimolar amounts of nitroalkene **1**, **2**, or **7** (1 mmol) and 2-propene-1-thiol (**15**) (0.13 mL, 1 mmol) in $CDCl_3$ (2 mL), Et_3N (0.01 mL, 0.1 mmol) was added, and the reaction mixture was stirred at 18.6 °C. ^{1}H NMR spectra were recorded at the same probe temperature (18.4 °C) by withdrawing aliquots (0.5 mL) after 4 min, which showed 69% conversion for **1**, 71% conversion for **2**, and 57% conversion for **7**.

Supporting Information (see footnote on the first page of this article): Details of the optimization of the level of theory and basis set, coordinates of optimized geometries, contour plots, table of NHO directionality and bond bending, correlations, and solvent model calculation results.

Acknowledgments

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[1] Reviews on conjugated nitroalkenes: a) O. M. Berner, L. Tedeschi, D. Enders, *Eur. J. Org. Chem.* **2002**, 1877; b) N. Kranse, A. Hoffmann-Röder, *Synthesis* **2001**, 171; c) A. G. M. Barrett, *Chem. Soc. Rev.* **1991**, *20*, 95; d) A. G. M. Barrett, G. G. Graboski, *Chem. Rev.* **1990**, *86*, 751; e) S. E. Denmark, A. Thorarensen, *Chem. Rev.* **1996**, *96*, 137; f) A. Yoshikoshi, M. Miyashita, *Acc. Chem. Res.* **1985**, *18*, 284; g) L. F. Tietze, G. Kettschau, *Top. Curr. Chem.* **1997**, *189*, 1; h) S. Rajappa, *Tetrahedron* **1981**, *37*, 1453; i) G. W. Kabalka, R. S. Varma, *Org. Prep. Proc. Int.* **1987**, *19*, 283.

[2] Reviews on nitro compounds: a) D. Seebach, E. W. Colvin, F. Lehr, T. Weller, *Chimia* **1979**, *33*, 1; b) J. P. Adams, D. S. Box, *J. Chem. Soc., Perkin Trans. 1* **1999**, 749; c) F. A. Luzzio, *Tetrahedron* **2001**, *57*, 915; d) Several articles in *Tetrahedron: Symposia in Print* **1990**, *46* (21) (Ed.: A. G. M. Barrett); e) S. L. Ioffe, L. M. Leont'eva, V. A. Tartakovskii, *Russ. Chem. Rev.* **1977**, *46*, 1658; f) *Nitro Compounds: Recent Advances in Synthesis and Chemistry* (Eds.: H. Feuer, A. T. Nielsen), VCH, Weinheim, **1990**; g) N. Ono in *The Nitro Group in Organic Synthesis*, Wiley-VCH, New York, **2001**; h) *The Chemistry of Amino, Nitroso, Nitro and Related Groups* (Ed.: S. Patai), Wiley, Chichester, **1996**; i) J. P. Adams, *J. Chem. Soc., Perkin Trans. 1* **2002**, 2586; j) G. Rosini, *Comprehensive Organic Synthesis* (Ed.: B. M. Trost), Pergamon, Oxford, **1991**, vol. 2, p. 321; k) R. Ballini, G. Bosica, D. Fiorini, A. Palmieri, M. Petrini, *Chem. Rev.* **2005**, *105*, 933.

[3] Selected articles: a) T. A. Johnson, D. O. Jang, B. W. Slafer, M. D. Curtis, P. Beak, *J. Am. Chem. Soc.* **2002**, *124*, 11689; b) G. H. Posner, R. D. Crouch, *Tetrahedron* **1990**, *46*, 7509; c) U. Jahn, D. Rudakov, *Synlett* **2004**, 1207; d) M.-C. Yan, Z. Tu, C. Lin, S. Ko, J. Hsu, C. F. Yao, *J. Org. Chem.* **2004**, *69*, 1565; e) I. N. N. Namboothiri, M. Ganesh, S. M. Mobin, M. Cojocaru, *J. Org. Chem.* **2005**, *70*, 2235.

[4] Reviews: a) I. N. N. Namboothiri, A. Hassner, *Top. Curr. Chem.* **2001**, *216*, 1 and references cited therein; b) A. Hassner, K. S. K. Murthy, R. Maurya, W. Dehaen, O. Friedman, *J. Hetrocycl. Chem.* **1994**, *31*, 687; c) see refs.[1c–1e]

[5] Selected articles: a) I. N. N. Namboothiri, A. Hassner, H. E. Gottlieb, *J. Org. Chem.* **1997**, *62*, 485; b) A. Hassner, O. Friedman, W. Dehaen, *Liebigs Ann./Recueil* **1997**, 587; c) P.-Y. Roger, A.-C. Durand, J. Rodriguez, J.-P. Dulcere, *Org. Lett.* **2004**, *6*, 2027; d) K. S.-L. Huang, E. H. Lee, M. M. Olmstead, M. J. Kurth, *J. Org. Chem.* **2000**, *65*, 499; e) D. G. J. Young, G. Gomez-Bengoa, A. H. Hoveyda, *J. Org. Chem.* **1999**, *64*, 692; f) D. Enders, A. Haertwig, J. Runsink, *Eur. J. Org. Chem.* **1998**, 1793; g) T. Ishikawa, T. Miyahara, M. Asakura, S. Higuchi, Y. Miyauchi, S. Saito, *Org. Lett.* **2005**, *7*, 1211; h) D. Seebach, M. A. Brook, *Helv. Chim. Acta* **1985**, *68*, 319; i) M. A. Brimble, A. D. Johnston, *Tetrahedron* **1994**, *50*, 4887; j) N. Latif, N. Mishriky, F. M. Assad, S. A. Meguid, *Ind. J. Chem.* **1982**, *21B*, 872; k) L. Gottlieb, A. Hassner, *J. Org. Chem.* **1995**, *60*, 3759; l) C. Yuan, C. Li, *Heteroat. Chem.* **1995**, *6*, 339.

[6] Selected recent articles: a) See ref.[3a]; b) D. Seebach, H. Schäfer, *Tetrahedron* **1995**, *51*, 2305; c) B. List, P. Pojarliev, H. J. Martin, *Org. Lett.* **2001**, *3*, 2423; d) T. Hayashi, T. Senda, M. Ogasawara, *J. Am. Chem. Soc.* **2000**, *122*, 10716; e) T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc.* **2003**, *125*, 12672; f) J. M. Betancort, K. Sakthivel, R. Thayumanavan, F. Tanaka, C. F. Barbas III, *Synthesis* **2004**, 1509; g) H. Choi, Z. Hua, I. Ojima, *Org. Lett.* **2004**, *6*, 2689; h) A. J. A. Cobb, D. A. Longbottom, D. M. Shaw, S. V. Ley, *Chem. Commun.* **2004**, 1808; i) T. Ishii, S. Fujioka, Y. Sekiguchi, H. Kotsuki, *J. Am. Chem. Soc.* **2004**, *126*, 9558; j) M. Watanabe, A. Ikagawa, H. Wang, K. Murata, T. Ikaria, *J. Am. Chem. Soc.* **2004**, *126*, 11148; k) D. M. Barnes, J. Ji, M. G. Fickes, M. A. Fitzgerald, S. A. King, H. E. Morton, F. A. Plagge, M. Preskill, S. H. Wagaw, S. J. Wittenberger, J. Zhang, *J. Am. Chem. Soc.* **2002**, *124*, 13097; l) P. Kotrusz, S. Toma, H.-G. Schmalz, A. Adler, *Eur. J. Org. Chem.* **2004**, 1577; m) J. Wu, D. M. Mampreian, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 4584; n) D. Polet, A. Alexakis, *Tetrahedron Lett.* **2005**, *46*, 1529; o) H. Li, Y. Wang, L. Tang, F. Wu, X. Liu, C. Guo, B. M. Foxman, L. Deng, *Angew. Chem. Int. Ed.* **2005**, *44*, 105; p) M. Yamashita, K. Yamada, K. Tomioka, *Tetrahedron* **2004**, *60*, 4237; q) A. Rimkus, N. Sewald, *Synthesis* **2004**, 135; r) A. Duursma, A. J. Minnaard, B. L. Feringa, *J. Am. Chem. Soc.* **2003**, *125*, 3700; s) J. Kang, J. H. Lee, D. S. Lim, *Tetrahedron: Asymmetry* **2003**, *14*, 305; t) A. P. Davis, K. J. Dempsey, *Tetrahedron: Asymmetry* **1995**, *6*, 2829.

[7] Selected articles: a) X. Yang, R. Wang, *Tetrahedron: Asymmetry* **1997**, *8*, 3275; b) M. Node, R. Kurosaki, K. Hosomi, I. Takehisa, K. Nishide, T. Ohmori, K. Fuji, *Tetrahedron Lett.* **1995**, *36*, 99; c) T. R. Kim, S. Y. Choi, *Bull. Kor. Chem. Soc.* **1981**, *2*, 125; d) G. Trewartha, J. N. Burrows, A. G. M. Barrett, *Tetrahedron Lett.* **2005**, *46*, 3553; e) J. Hubner, J. Liebscher, M. Patzel, *Tetrahedron* **2002**, *58*, 10485; f) D. Lucet, P. Heyse, A. Gissot, T. Le Gall, C. Mioskowski, *Eur. J. Org. Chem.* **2000**, 3575; g) M. Ayerbe, I. Morao, A. Arrieta, A. Linden, F. P. Cossio, *Tetrahedron Lett.* **1996**, *37*, 3055.

[8] a) See ref.[1a]; b) L. Zu, H. Li, J. Wang, X. Yu, W. Wang, *Tetrahedron Lett.* **2006**, *47*, 5131; c) J. Wang, H. Li, B. Lou, L. Zu, H. Guo, W. Wang, *Chem. Eur. J.* **2006**, *12*, 4321; d) D. A. Yala-

lov, S. B. Tsogoeva, S. Schmatz, *Adv. Synth. Catal.* **2006**, *348*, 826; e) S. B. Tsogoeva, S. Wei, *Chem. Commun.* **2006**, *13*, 1451; f) S. Luo, X. Mi, L. Zhang, S. Liu, H. Xu, J.-P. Cheng, *Angew. Chem. Int. Ed.* **2006**, *45*, 3093; g) N. Mase, K. Watanabe, H. Yoda, K. Takabe, F. Tanaka, C. F. Barbas III, *J. Am. Chem. Soc.* **2006**, *128*, 4966; h) V. Rai, S. M. Mobin, I. N. N. Namboothiri, *231st ACS National Meeting*, ORGN 37, Abstracts of Papers, Atlanta, GA, USA, March 26–30, **2006**.

[9] a) See ref.[6b]; b) I. N. N. Namboothiri, A. Hassner, *J. Organomet. Chem.* **1996**, *518*, 69 and the references cited therein; c) C.-M. Chu, J.-T. Liu, W.-W. Lin, C.-F. Yao, *J. Chem. Soc., Perkin Trans. 1* **1999**, 47.

[10] a) K. Morita, Z. Suzuki, H. Hirose, *Bull. Chem. Soc. Jpn.* **1968**, *41*, 815; b) A. B. Baylis, M. E. D. Hillman, *Ger. Offen.* **1972**, DE2155113 (*Chem. Abstr.* **1972**, *77*, 434174); M. E. D. Hillman, A. B. Baylis, *U.S. Patent* **1973**, 3743669; for recent reviews, see: c) D. Basavaiah, A. J. Rao, T. Satyanarayana, *Chem. Rev.* **2003**, *103*, 811; d) P. Langer, *Organic Synthesis Highlights V* (Eds.: H.-G. Schmalz, T. Wirth), Wiley-VCH, Weinheim, Germany, **2003**, p. 165; see also: e) T. Kataoka, H. Kinoshita, *Eur. J. Org. Chem.* **2005**, 45.

[11] For recent reports on the MBH reaction of nitroalkenes, see: a) I. Deb, M. Dadwal, S. M. Mobin, I. N. N. Namboothiri, *Org. Lett.* **2006**, *8*, 1201; b) M. Dadwal, R. Mohan, D. Panda, S. M. Mobin, I. N. N. Namboothiri, *Chem. Commun.* **2006**, 338; c) N. Rastogi, I. N. N. Namboothiri, *Tetrahedron Lett.* **2004**, *45*, 4745; d) M. Dadwal, S. M. Mobin, I. N. N. Namboothiri, *Org. Biomol. Chem.* **2006**, 338; for a related work, see: e) R. Ballini, L. Barboni, G. Bosica, D. Fiorini, E. Mignini, A. Palmieri, *Tetrahedron* **2004**, *60*, 4995.

[12] a) C. F. Bernasconi, R. A. Renfrow, P. R. Tia, *J. Am. Chem. Soc.* **1986**, *108*, 4541; b) C. F. Bernasconi, *Tetrahedron* **1989**, *45*, 4017 and references cited therein.

[13] S. Hoz, Z. Gross, *J. Am. Chem. Soc.* **1988**, *110*, 7489.

[14] K. Ananthakumar, A. Sarathi, C. Gnanasekaran, A. Shunmugasundaram, *Indian J. Chem.* **2003**, *42B*, 1943.

[15] P. Mondal, K. K. Hazarika, R. C. Deka, *Phys. Chem. Commun.* **2003**, *6*, 24.

[16] a) L. R. Domingo, P. Perez, R. Contreras, *Tetrahedron* **2004**, *60*, 6585; b) L. R. Domingo, *Eur. J. Org. Chem.* **2004**, 4788.

[17] a) J. P. Foster, F. A. Weinhold, *J. Am. Chem. Soc.* **1980**, *102*, 7211; b) A. E. Reed, F. A. Weinhold, *J. Am. Chem. Soc.* **1985**, *89*, 2688; c) A. E. Reed, F. A. Weinhold, R. Weiss, J. Macheleid, *J. Phys. Chem.* **1985**, *89*, 2688; d) A. E. Reed, R. B. Weinstock, F. A. Weinhold, *J. Chem. Phys.* **1985**, *83*, 735; e) A. E. Reed, F. A. Weinhold, *J. Phys. Chem.* **1986**, *84*, 2428; f) A. E. Reed, F. A. Weinhold, *J. Am. Chem. Soc.* **1986**, *108*, 3586; g) J. T. Nelson, W. J. Pietro, *Inorg. Chem.* **1989**, *28*, 544.

[18] a) S. Woodward, *Tetrahedron* **2002**, *58*, 1017 and the references cited therein; b) A. K. Chandra, M. T. Nguyen, *Int. J. Mol. Sci.* **2002**, *3*, 310.

[19] a) R. G. Parr, W. Yang, *Density Functional Theory of Atoms and Molecules*, Oxford University Press, Oxford, **1989**; b) R. G. Parr, W. Yang, *Ann. Rev. Phys. Chem.* **1995**, *46*, 701.

[20] a) G. Madzarova, A. Tadzer, Tz. P. Cholakova, A. A. Dobrev, T. Mineva, *J. Phys. Chem. A* **2005**, *109*, 387 and references cited therein; b) C. Spino, H. Rezaei, Y. L. Dory, *J. Org. Chem.* **2004**, *69*, 757; c) J. Melin, F. Aparicio, V. Subramanian, M. Galvan, P. K. Chattaraj, *J. Phys. Chem. A* **2004**, *108*, 2487; d) G. Roos, S. Loverix, F. De Proft, L. Wyns, P. Geerlings, *J. Phys. Chem. A* **2003**, *107*, 6828; e) H.-T. Chen, J.-J. Ho, *J. Phys. Chem. A* **2003**, *107*, 7643; f) G. I. Ca'rdenas-Jiro'n, E. Parra-Villalobos, *J. Phys. Chem. A* **2003**, *107*, 11483; g) P. K. Chattaraj, B. Maiti, *J. Am. Chem. Soc.* **2003**, *125*, 2705; h) B. Gomez, P. K. Chattaraj, E. Chamorro, R. Contreras, P. Fuentealba, *J. Phys. Chem. A* **2002**, *106*, 11233; i) K. R. S. Chandrakumar, S. Pal, *J. Phys. Chem. A* **2002**, *106*, 11775; j) J. Olah, C. V. Alsenoy, A. B. Sannigrahi, *J. Phys. Chem. A* **2002**, *106*, 3885; k) P. K. Chattaraj, *J. Phys. Chem. A* **2001**, *105*, 511; l) M. V. Lebedev, *J. Phys. Chem. B* **2001**, *105*, 511; m) S. Pal, K. R. S. Chandrakumar, *J. Am. Chem. Soc.* **2000**, *122*, 4145; n) R. G. Parr, L. von Szentpaly, S. Liu, *J. Am. Chem. Soc.* **1999**, *121*, 1922; o) J. Padmanabhan, R. Parthasarathy, V. Subramanian, P. K. Chattaraj, *J. Phys. Chem. A* **2006**, *110*, 2739; p) W. Kohn, A. D. Becke, R. G. Parr, *J. Phys. Chem.* **1996**, *100*, 12974; q) B. Pinter, F. De Proft, T. Veszpremi, P. Geerlings, *J. Chem. Sci.* **2005**, *117*, 561; r) F. De Proft, C. Van Alsenoy, P. Geerlings, *J. Phys. Chem.* **1996**, *100*, 7440.

[21] a) H. Chermette, *J. Comput. Chem.* **1999**, *20*, 129; b) T. Mineva, N. Neshev, N. Russo, E. Silicia, M. Toscano, *Adv. Quant. Chem.* **1999**, *33*, 273; c) P. Geerlings, F. De Proft, W. Langenaekar, *Adv. Quant. Chem.* **1999**, *33*, 301; d) F. De Proft, P. Geerlings, *Chem. Rev.* **2001**, *101*, 1451.

[22] a) R. Meza, B. Gordillo, M. Galvan, *Int. J. Quant. Chem.* **2005**, *104*, 29; b) see ref.[15]; c) see ref.[16a]

[23] a) J. Poater, M. Duran, M. Sola, B. Silvi, *Chem. Rev.* **2005**, *105*, 3911 and the references cited therein; b) R. H. Mitchell, *Chem. Rev.* **2001**, *101*, 1301; c) see ref.[21d]

[24] R. G. Parr, R. G. Pearson, *J. Am. Chem. Soc.* **1983**, *105*, 7512.

[25] See ref.[20n]

[26] a) R. G. Parr, W. Yang, *J. Am. Chem. Soc.* **1984**, *106*, 4049; b) W. Yang, R. G. Parr, *Proc. Natl. Acad. Sci.* **1985**, *82*, 6723.

[27] See ref.[20k]

[28] a) W. Yang, W. J. Mortier, *J. Am. Chem. Soc.* **1986**, *108*, 5708; b) L. R. Domingo, M. Arno, R. Contreras, P. Perez, *J. Phys. Chem. A* **2002**, *106*, 952.

[29] P. Perez, *J. Phys. Chem. A* **2003**, *107*, 522.

[30] P. Perez, A. Toro-Labbe, A. Aizman, R. Contreras, *J. Org. Chem.* **2002**, *67*, 4747.

[31] L. R. Domingo, M. J. Aurell, P. Perez, R. Contreras, *J. Phys. Chem. A* **2002**, *106*, 6871.

[32] a) Ref.[13]; b) S. Hoz, *J. Org. Chem.* **1982**, *47*, 3545; c) S. Hoz, D. Speizman, *J. Org. Chem.* **1983**, *48*, 2904.

[33] Since electronic distribution is mainly responsible for atomic charges, and the former can be characterized in terms of NMR chemical shifts, the theoretical level that was found suitable for calculating the chemical shift values was used for calculating the natural charges, as well. This is despite the fact that chemical shifts are also dependent on other factors, such as diamagnetic effects, which will not contribute to the atomic charges but could influence the chemical shifts. However, the magnitude of this electron density is determined by the extent of delocalization in the system, which is again responsible for atomic charges. Therefore, the change in chemical shifts due to a diamagnetic effect, in all probability, will be proportional to the change in atomic charges. See several reviews in *Chem. Rev.* **2001**, *101* that discuss aromaticity, ring current, structural aspects, and DFT at conceptual and computational levels.

[34] Although the geometry varies considerably within nitroalkenes, the opposite polarization of the C-α–C-β bond in β-nitrostyrene (**1**) and 1-(2-furyl)-2-nitroethylene (**8**) is not attributable to geometric features, because benzene and furan rings in **1** and **8**, respectively, have similar σ-bond bendings (Table S1, Supporting Information).

[35] Second-order perturbation analysis shows that the hyperconjugative contribution towards the C-α–C-β bond by four allylic hydrogen atoms is 2.82 kcal mol^{-1}, which is far less than the contribution of the phenyl ring in β-nitrostyrene (**1**, 14.1 kcal mol^{-1}). The contribution of the *trans* H atom in nitroethylene (**14**) towards the C-α–C-β bond is only 0.13 kcal mol^{-1}.

[36] a) R. G. Pearson, *Chemical Hardness: Application from Molecules to Solid*, Wiley-VCH, Weinheim, **1997**; b) K. D. Sen, D. M. P. Mingos, *Chemical Hardness: Structure and Bonding*, Springer, Berlin, **1993**, vol. 80; c) See ref.[18a]

[37] K. Fukui, *Science* **1982**, *218*, 747.

[38] a) NMR spectra (^{1}H) were recorded with an AMX-400 or VXR-300S spectrometer with TMS as the internal standard. For reports on the Michael addition of 2-propene-1-thiol to nitroalkenes, see: b) A. Hassner, W. Dahaen, *J. Org. Chem.*

1990, *55*, 5505; c) W. Dahaen, A. Hassner, *Tetrahedron Lett.* **1990**, *31*, 743.

[39] M.-C. Yan, Z. Tu, C. Lin, S. Ko, J. Hsu, C.-F. Yao, *J. Org. Chem.* **2004**, *69*, 1565.

[40] G. Bartoli, M. Bosco, S. Giuli, A. Giuliani, L. Lucarelli, E. Marcantoni, L. Sambri, E. Torregiani, *J. Org. Chem.* **2005**, *70*, 1941.

[41] T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc.* **2003**, *125*, 12672.

[42] E. Licandro, S. Maiorana, L. Capella, R. Manzotti, A. Papagni, B. Vandoni, A. Albinati, S. H. Chuang, J.-R. Hwu, *Organometallics* **2001**, *20*, 485.

[43] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery Jr, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, N. Rega, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, J. A. Pople, *Gaussian 98*, revision A.11.4, Gaussian, Inc., Pittsburgh, PA, **2002**..

[44] a) C. J. Cramer, *Essentials of Computational Chemistry: Theories and Models*, John Wiley & Sons, Chichester, UK, **2003**; b) A. R. Leach, *Molecular Modelling: Principles and Applications*, 2nd ed., Pearson Education, Prentice Hall, Harlow, UK, **2003**.

[45] a) See ref.[19a]; b) see ref.[20n]; c) L. von Szentpaly, *J. Phys. Chem. A* **1998**, *102*, 10912; d) L. von Szentpaly, *Chem. Phys. Lett.* **1995**, *245*, 209; e) L. von Szentpaly, *J. Mol. Struct. (THEOCHEM)* **1991**, *233*, 71.

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