

DFT studies on structure and spectroscopic properties of α,β -unsaturated ester dipolarophiles; Application in prediction of their reactivities with *C*-phenyl-*N*-methyl nitrone

Anindita Ghosh, Avijit Banerji* and Julie Banerji

Centre of Advanced Studies on Natural Products including Synthesis, Department of Chemistry,
University College of Science and Technology, Kolkata-700 009, India

E-mail : ablabcu@yahoo.co.uk; banerjijulie@yahoo.com

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Abstract : The optimized geometries, electrostatic potential maps, FMO energies, electronic chemical potentials, chemical hardness, chemical softness, global and local electrophilicity indices and Fukui indices of a number of α,β -unsaturated esters have been calculated at DFT/B3LYP/6-31++G(d,p) level of theory. DFT/B3LYP/6-311++G(d,p) calculated ^1H NMR and experimentally recorded chemical shift values show good agreement. The fundamental vibrational modes have been assigned by comparing the theoretically computed and experimental frequencies. The thermodynamic parameters are also presented. The calculated reactivity indices have been used to predict regioselectivities of these unsaturated esters as dipolarophiles with *C*-phenyl-*N*-methyl nitrone.

Keywords : α,β -Unsaturated esters, geometry optimization, FMO, DFT, reactivity indices, 1,3-DC.

Introduction

α,β -Unsaturated esters are an important class of compounds, which are of synthetic importance^{1,2} – these undergo Diels-Alder and 1,3-dipolar cycloadditions², Michael additions and related nucleophilic attack at the β -position. Hence calculations regarding their molecular geometries, frontier orbital energies and reactivity indices are of value in analyzing and predicting their reactivity and selectivity profiles. Our interest in these molecules basically stem from our studies on 1,3-dipolar cycloadditions, particularly of nitrones, to conjugated olefinic systems, which constitute a major route to five membered heterocyclic ring systems³. We have reported the optimized geometries, FMO energies and spectroscopic characteristics of nitrones and other 1,3-dipoles^{4,5}. Good agreement was obtained for computed molecular geometry of *N*-methyl-*C*-phenyl nitrone with that determined by X-ray crystallographic studies, and between theoretically computed values with those experimentally obtained for spectroscopic measurements (IR, NMR)⁵. Recently, we have reported experimental and theoretical aspects of nitrone cycloaddi-

tions to crotonate esters⁶ as well as experimental and theoretical studies on cycloadditions of acyclic and cyclic nitrones to α,β -unsaturated ketones^{7,8}. Other recent communications have reported DFT calculations at different levels to rationalize the observed selectivities of 1,3-dipolar cycloadditions in terms of the free energies of activation, frontier molecular orbital energies of reactants and reactivity indices of the reactants⁹⁻¹¹.

The present communication deals with theoretical computations for α,β -unsaturated esters, which are important dipolarophiles in which the double bond is conjugated with electron-withdrawing ester groups. Computations have been carried out for methyl acrylate (**1**), methyl cinnamate {*cis*- (**2**) and *trans*- (**3**)}, dimethyl methylene malonate (**4**) and dimethyl benzylidene malonate (**5**).

Experimental

Dimethyl benzylidene malonate (**4**) was obtained by following the standard laboratory procedure¹² given for diethyl benzylidene malonate, substituting an equivalent

amount of dimethyl malonate in place of diethyl malonate as starting material. Its IR spectrum was recorded in KBr pellet using a Perkin-Elmer RX-9 FT-IR spectrophotometer with a resolution of 1 cm^{-1} . ^1H NMR spectrum of (4) was analysed in CDCl_3 solution using Bruker AV-300 NMR spectrophotometer. Chemical shifts for ^1H NMR are reported in parts per million downfield from tetramethylsilane (TMS).

Computational methods

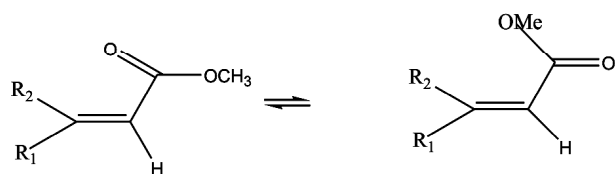
The molecular geometries of the dipolarophiles (1), (2), (3), (4) and (5) were optimized by Density Functional Theory with Becke's¹³ three-parameter hybrid exchange functional in combination with the gradient-corrected correlation functional of Lee, Yang, and Parr¹⁴ (B3LYP) using 6-311++G(d,p) basis set. *C*-Phenyl-*N*-methyl nitron was also optimized by B3LYP using same basis set, viz. 6-311++G(d,p). The frequency calculations and infra-red intensities were calculated by restricted (closed shell) DFT/B3LYP method using 6-311++G(d,p) basis set. Theoretical NMR calculations benefit from an accurate geometry and a large basis set – Cheeseman *et al.*¹⁵ considered B3LYP/6-31G(d) optimised structures to be the minimum recommended model chemistry for predicting NMR properties. In the present work GIAO/SCF ^1H NMR calculations of the dipolarophiles were carried out at B3LYP level using an extended 6-311++G(d,p) basis set.

All calculations were carried out on a personal computer using Gaussian 2003¹⁶ set of programs along with the graphical interface Gauss View 2003.

Results and discussion

(a) Molecular geometry

The α,β -unsaturated methyl esters can exist in *s-cis* and *s-trans* forms (Fig. 1). Recently, Abraham *et al.*¹⁷



- (1) Methyl acrylate $R_1 = R_2 = \text{H}$
 (2) *cis*-Methyl cinnamate $R_1 = \text{H}, R_2 = \text{Ph}$
 (3) *trans*-Methyl cinnamate $R_1 = \text{Ph}, R_2 = \text{H}$

Fig. 1. Conformers of α,β -unsaturated esters.

has reported investigations of the configuration and conformations of some α,β -unsaturated carbonyl compounds on the basis of lanthanide induced ^{13}C NMR shifts together with computational studies (MMFF94, RHF/6-31G, RHF/6-311G(d,p) and B3LYP/6-311G(d,p)). They reported that both *s-cis* and *s-trans* forms are present for aldehydes, methyl vinyl ketone, methyl crotonate, *trans*-cinnamaldehyde, *trans*-cinnamyl methyl ketone and *trans*-methyl cinnamate.

Our present computational work on the unsaturated esters were carried out with an extended basis set at the B3LYP/6-311++G(d,p) level. The results are discussed briefly; references to relevant earlier work are made wherever appropriate.

Methyl acrylate (1) – The molecular geometry and conformational analysis of methyl acrylate has been the subject of intense study since 1967 [see Refs. 17, 18 for earlier references cited therein]. Egawa *et al.*¹⁸ carried out a detailed investigation by gas phase electron diffraction study augmented by *ab initio* calculations at the HF/4-31G(d) level and rotational constants. They estimated *s-cis* : *s-trans* ratio of $67(\pm 11) : 33$ at $20\text{ }^\circ\text{C}$, corresponding to a free energy difference $\Delta G = 1.7(+1.4; -1.2)$ kcal; their experimental results¹⁸ and the theoretically calculated values by HF/4-31G(d) calculations are given alongside our calculations in Table 1. Our computational results, show closer correspondence to the experimental values (Table 1). The theoretically computed structure of methyl acrylate shows that the molecule is coplanar with two of the hydrogens of the methoxy group

Table 1. Structural parameters of methyl acrylate (1)

Bond length	<i>s-cis</i> ^a (1b)	<i>s-trans</i> ^a (1a)
r(C=C)	1.332	1.332
r(C=O)	1.209	1.210
r(C-C)	1.484	1.482
r(C=O-O)	1.352	1.350
r(O-CH ₃)	1.438	1.438
Bond angle	<i>s-cis</i> ^a	<i>s-trans</i> ^a
C=C-C	121.0°	124.8°
C-C=O	126.0°	123.4°
C-C-O	110.5°	113.2°
C-O-C	116.0°	115.9°

Bond distances in Angstroms and bond angles in degrees.

^aComputed by B3LYP/6-311++G(d,p) in the present work.

having torsion angles $\pm 60^\circ$ from the molecular plane. The difference in energy between *s-cis* and *s-trans* forms was calculated to be 1.9139 kcal/mole in our present work.

Methyl cinnamate – The computations were carried out in four sets : two conformations (carbonyl *s-cis* and *s-trans*) of each of the two configurations of *cis*- (**2a**, **2b**) and *trans*- (**3a**, **3b**) methyl cinnamate.

Dimethyl methylenemalonate (**4**) and *dimethyl benzyldenemalonate* (**5**) : Computations were also carried out for dimethyl methylenemalonate¹⁹ (**4**) and dimethyl benzyldene malonate (**5**).

The calculated molecular geometries are shown in Fig. 2, along with the numbering system used in the computational studies. Salient data regarding bond lengths, bond angles and torsional angles for the compounds are collected in Table 2.

The molecular geometry for methyl cinnamate has been computed for *trans* and *cis* configurations, with *s-cis* and *s-trans* carbonyl conformations for each. In (**3a**) and (**3b**) the molecular plane encompasses the phenyl ring, the double bond, the carbonyl group and the C-O-C bond. This planarity is lost in both conformers of *cis*-methyl cinnamate due to steric interactions of the side chain with the phenyl group. In *s-cis* conformation (**2a**), the plane defined by the olefinic bond (C3-C19-C13=C16-H15) is twisted by $\sim 10^\circ$ from the average plane defined by the ring. In *s-trans* (**2b**), there is a greater deviation of about 38° from planarity of the olefinic bond with the phenyl ring, due to fairly severe steric interaction with the methoxy group. For dimethyl methylenemalonate (**4**), the calculated molecular geometry corresponding to minimized energy (Fig. 2, Table 2) shows that the double bond and the plane of the two carbonyl groups are twisted by $\sim 29^\circ$ in mutually opposite directions, with the two carbonyl groups pointing in opposite directions to minimize dipolar and steric interactions. In dimethyl benzyldenemalonate (**5**), while the phenyl ring and the *trans*-carbomethoxy group are almost coplanar, the second carbomethoxy group (*cis* to the phenyl group) is approximately perpendicular to the rest of the molecular plane, and thus effectively out of conjugation. This is reflected in the difference in bond lengths of the carbonyls, as well as C14-C15 and C14-C16 bonds of the two carbomethoxyl groups.

(b) Frontier Molecular Orbital energies

Frontier molecular orbital energies have been employed by Fukui^{20,21} and others to explain reactivities and regioselectivities. The HOMO and LUMO energies of the dipolarophiles (**1-5**) have been calculated at the DFT/B3LYP/6-311++G(d,p) level; these are presented in Fig. 3, which also shows the MO surfaces. The HOMO-LUMO gap is a measure of the chemical hardness η . Additional conjugation of the phenyl groups raises the HOMO energy, and lowers the LUMO energy from methyl acrylate to methyl cinnamate. HOMO energy is raised by ~ 0.040 a.u. for all four forms (**2a**, **2b**, **3a**, **3b**). The corresponding HOMO-LUMO gap diminishes by 0.226 a.u. in methyl acrylate to 0.177 a.u. in (**2a**), and further to 0.168 a.u. in (**2b**), (**3a**), (**3b**). The introduction of the second carbomethoxy group in dimethyl benzyldenemalonate (**5**), which is virtually perpendicular to the rest of the molecule in **5**, has only a small effect on Frontier orbital energies on compared to **3a**, **3b**.

(c) Vibrational assignments

In order to obtain a more complete description of molecular motion, vibrational frequency calculations have been carried out. The vibrational analysis also yields the detailed information about the intramolecular vibrations in the molecular fingerprint region. The thermochemistry predicted by the vibrational frequency calculations are utilised to determine the entropies, enthalpies and free energies of activations during 1,3-dipolar cycloadditions of nitrones and other reactions. The degree of precision of the calculated thermodynamic parameters can be verified by comparing the theoretical and experimental vibrational frequencies. The vibrational frequencies of (**4**) and (**5**) have been calculated at DFT/B3LYP level using 6-311++G(d,p) basis set. The calculated frequencies were scaled down by a factor of 0.9613 recommended for DFT/B3LYP/6-311++G(d,p) calculations²². The vibrational frequencies of *C*-phenyl-*N*-methyl nitron have been reported in our earlier papers at DFT/B3LYP level using 6-311++G(d,p) basis set⁵. The vibrational frequency assignments have been carried out by combining the results of the Gaussview program and symmetry considerations. Detailed analysis of the IR spectrum of methyl acrylate (**1**) has been reported earlier by a number of groups with computations at different levels^{17,18}; hence,

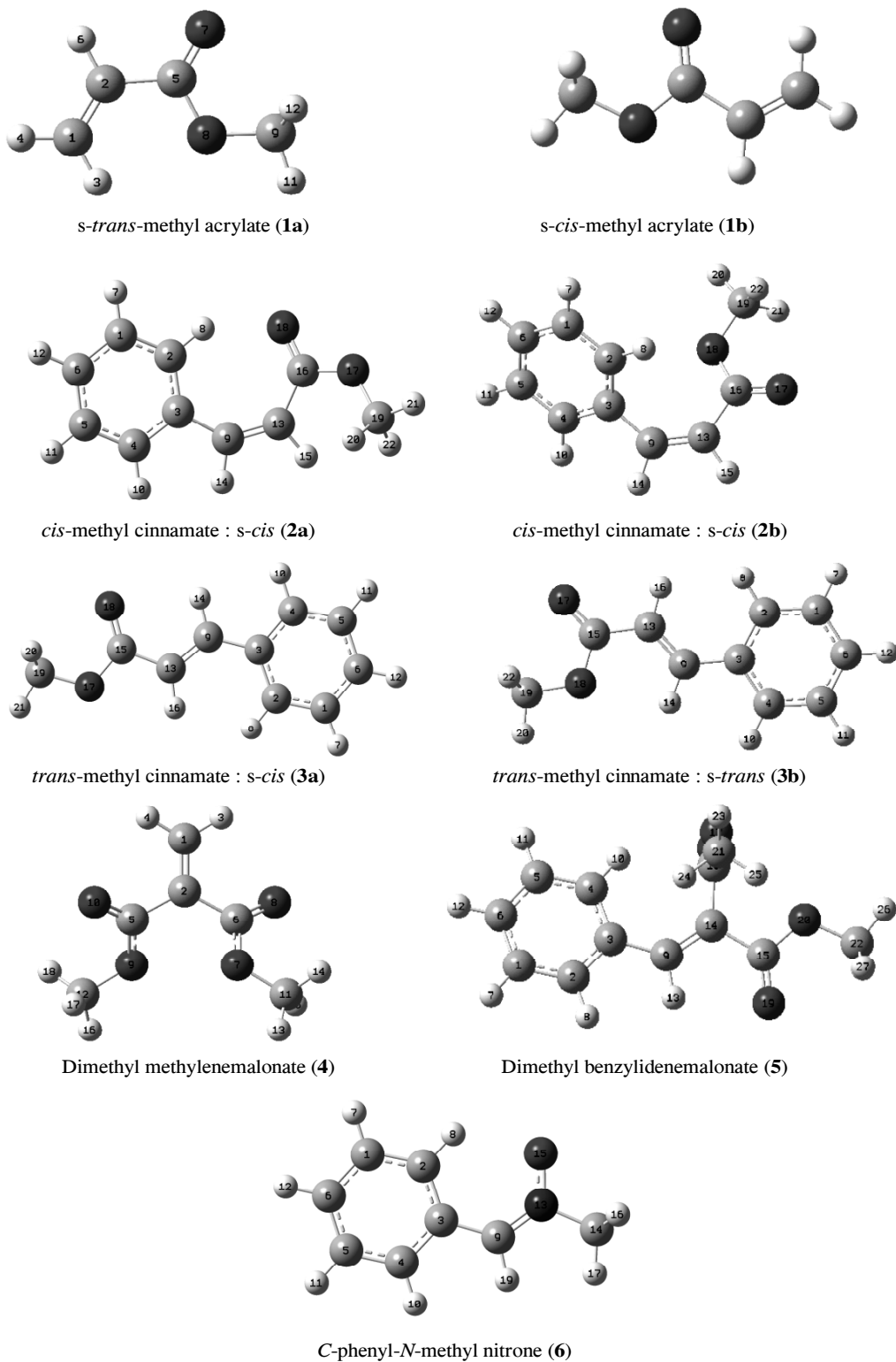


Fig. 2. Optimized molecular geometries of (1) to (6) with numbering schemes.

Table 2. Structural parameters of dipolarophiles (**1-5**)

Compounds	Bond distances in Angstroms (Å); bond and torsional angles in degrees					
	Bond length		Bond angle		Torsional angle	
Methyl acrylate (1)	C1-C2	1.332	H4-C1-C2	121.45	H3-C1-C2-H6	-180.00
	C2-C5	1.483	H3-C1-C2	120.95	H4-C1-C2-H6	0.00
	C5-O7	1.210	C1-C2-H6	121.79	C1-C2-H5-O7	-180
	C5-O8	1.350	C1-C2-C5	124.85	C2-C5-O8-C9	180
			H6-C2-C5	113.36	C5-O8-C9-H11	-179.90
			C2-C5-O8	31.61	C5-O8-C9-H12	60.53
			C2-C5-O7	123.42	C5-O8-C9-H10	-180.0
			O7-C5-O8	123.33		
			C5-O8-C9	33.20		
	<i>cis</i> -Methyl cinnamate with -C=O <i>s-cis</i> to aromatic ring (2a)	C9-C13	1.352	C2-C3-C9	125.97	C1-C2-C3-C9
C9-H14		1.089	C9-C3-C4	116.02	C2-C3-C4-H10	179.40
C13-H15		1.084	C3-C9-C13	135.64	C2-C3-C9-H14	-170.54
C13-C16		1.481	C3-C9-H14	111.43	C2-C3-C9-C13	-170.66
C16-O17		1.364	C13-C9-H14	111.87	C4-C3-C9-C13	-167.67
C16-O18		1.208	C9-C13-H15	115.06	C9-C13-C16-O18	-28.51
			C9-C13-C16	130.10	C9-C13-C16-O17	154.11
			H15-C13-C16	114.84	H15-C13-C16-O18	151.66
			C13-C16-O17	113.62		
			C13-C16-O18	126.00		
<i>cis</i> -Methyl cinnamate with -C=O <i>s-trans</i> to aromatic ring (2b)	C9-C13	1.345	C2-C3-C9	123.25	C1-C2-C3-C9	-177.74
	C9-H14	1.089	C9-C3-C4	118.32	C2-C3-C4-H10	178.38
	C13-C15	1.084	C3-C9-C13	131.88	C2-C3-C9-H14	141.36
	C13-H16	1.481	C3-C9-H14	113.37	C2-C3-C9-C13	-37.98
	C16-O17	1.212	C13-C9-H14	114.75	C4-C3-C9-C13	145.68
	C16-O18	1.349	C9-C13-H15	117.86	C9-C13-C16-O18	-21.56
			C9-C13-C16	131.06	C9-C13-C16-O17	12.54
			H15-C13-C16	111.07	H15-C13-C16-O18	158.05
			C13-C16-O17	122.57		
			C13-C16-O18	114.34		
<i>trans</i> -Methyl cinnamate with -C=O <i>s-cis</i> to aromatic ring (3a)	C9-C13	1.342	C2-C3-C9	123.23	C1-C2-C3-C9	-180.00
	C9-C14	1.087	C9-C3-C4	118.59	C2-C3-C4-H10	180.00
	C13-C15	1.475	C3-C9-C13	127.68	C2-C3-C9-H14	-179.98
	C13-C16	1.083	C3-C9-H14	115.84	C2-C3-C9-C13	0.01
	C15-C17	1.356	C13-C9-H14	116.47	C4-C3-C9-C13	-179.99
	C15-C18	1.211	C9-C13-H15	31.33	C9-C13-C15-O18	0.01
			C9-C13-C16	123.18	C9-C13-C15-C17	-179.96
			C15-C13-C16	116.39	H16-C13-C15-O18	-180.00
			C13-C15-O17	110.54		
			C13-C15-O18	126.40		
		O17-C15-O18	123.06			

Table-2 (contd.)

<i>trans</i> -Methyl cinnamate with -C=O <i>s-trans</i> to aromatic ring (3b)	C9-C13	1.343	C2-C3-C9	123.31	C1-C2-C3-C9	-179.99
	C9-C14	1.086	C9-C3-C4	118.54	C2-C3-C4-H10	-180.0
	C13-C15	1.474	C3-C9-C13	127.22	C2-C3-C9-H14	179.97
	C13-C16	1.083	C3-C9-H14	115.36	C2-C3-C9-C13	-0.08
	C15-C17	1.213	C13-C9-H14	117.42	C4-C3-C9-C13	179.99
	C15-C18	1.355	C9-C13-H15	124.46	C9-C13-C15-O18	-0.20
			C9-C13-C16	122.57	C9-C13-C15-C17	179.80
			C15-C13-C16	122.97	H16-C13-C15-O18	179.83
			C13-C15-O17	123.56		
			C13-C15-O18	31.65		
			O17-C15-O18	122.89		
			H4-C1-C2	120.51	H3-C1-C2-C6	2.10
	Dimethyl methylene malonate (4)	C2-C5	1.500	H3-C1-C2	120.51	H4-C1-C2-C6
C6-O7		1.344	C1-C2-C6	118.80	C1-C2-C5-O7	11.67
C6-O8		1.208	C1-C2-C5	118.80	C1-C2-C6-O8	-28.84
			C5-C2-C6	122.39	C2-C6-O7-C11	-178.52
			C2-C5-O9	111.80	C6-O7-C11-C15	-60.22
			C2-C5-O10	124.26	C6-O7-C11-C13	-179.74
			O9-C5-O10	123.85	C6-O7-C11-C14	60.64
			C5-O9-C12	115.96	C1-C2-C5-O10	-28.85
					H4-C1-C2-C5	-2.10
					C2-C5-O9-C12	-178.54
Dimethyl benzylidene malonate (5)	C9-C13	1.348	C4-C3-C9	124.71	C5-C4-C3-C9	-179.39
	C9-C13	1.088	C9-C3-C2	117.10	C4-C3-C2-H8	-178.90
	C14-C15	1.490	C3-C9-C14	131.20	C4-C3-C9-H13	-166.43
	C14-C16	1.509	C3-C9-H13	114.76	C4-C3-C9-C14	-6.20
	C15-C19	1.207	C13-C9-H14	114.02	C2-C3-C9-C13	13.09
	C15-C20	1.350	C9-C14-H15	117.50	C9-C14-C15-O20	-174.70
			C9-C14-C16	125.42	C9-C14-C15-O19	4.49
			C15-C14-C16	116.97	C16-C14-C15-O20	9.02
			C14-C15-O19	125.72	C9-C14-C16-O18	-86.48
			C14-C15-O20	110.71	C9-C14-C15-O17	92.72
			O19-C15-O20	123.56		

these have not been reported here. The experimental and scaled calculated wave numbers of dimethyl benzylidenemalonate (**5**) along with their respective modes are presented in Table 3. In general, a good agreement between experimental and calculated normal modes of vibrations has been observed. The normal modes of vibration have been calculated also for dimethyl methylene malonate (**4**) – though reports of its physical data are absent¹⁹. For (**4**), the C=C and C=O vibrations have been computed as 1612 and 1710 cm⁻¹ respectively. In *trans*-methyl cinnamate, *s-trans* (**3b**), the C=C and C=O vibrations have been computed at 1611 and 1686 (for *s-*

cis **3a** at 1613, 1692) cm⁻¹ respectively; experimental values are 1640, 1663, 1722 cm⁻¹. These compare with reported values of 1755 and 1642 cm⁻¹ in methyl acrylate¹⁸.

(d) NMR studies

The 300 MHz ¹H NMR spectra of the dipolarophiles show certain common characteristic features. NMR investigations of *C*-aryl-*N*-methyl nitrones have been reported earlier by us⁵. The theoretically computed GIAO nuclear magnetic shielding tensors (relative to TMS) of (**1**), (**3**), (**4**), and (**5**) are given in Table 4. For methyl

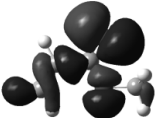

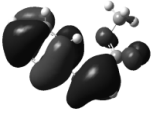
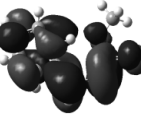

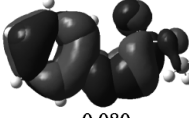
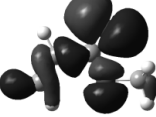
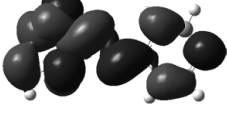
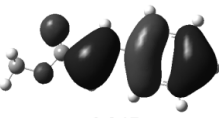

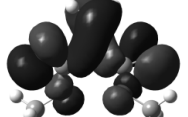
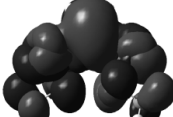
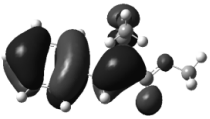
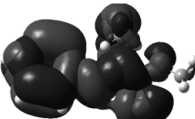
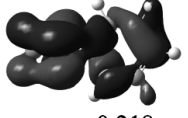
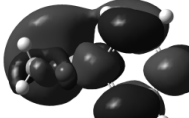
Compounds	HOMO orbitals; energy in a.u.	LUMO orbitals; energy in a.u.	HOMO-LUMO- energy gap in a.u. (eV)
Methyl acrylate (1)	 -0.289	 -0.063	0.226 (5.212 eV)
<i>cis</i> -Methyl cinnamate with -OMe <i>s-cis</i> to aromatic ring	 -0.249	 -0.072	0.177 (4.082 eV)
<i>cis</i> -Methyl cinnamate with -OMe <i>s-trans</i> to aromatic ring	 -0.249	 -0.080	0.169 (3.897 eV)
<i>trans</i> -Methyl cinnamate with -OMe <i>s-cis</i> to aromatic ring	 -0.248	 -0.079	0.169 (3.897 eV)
<i>trans</i> -Methyl cinnamate with -OMe <i>s-trans</i> to aromatic ring	 -0.247	 -0.079	0.168 (3.874 eV)
Dimethyl methylene malonate	 -0.279	 -0.075	0.204 (4.704 eV)
Dimethyl benzylidene malonate	 -0.253	 -0.088	0.165 (3.805 eV)
<i>C</i> -Phenyl- <i>N</i> -methyl nitrone	 -0.218	 -0.064	0.154 (3.551 eV)

Fig. 3. HOMO-LUMO energy of different dipolarophiles (1-5) and nitrone (6); with calculated energies in a.u.

acrylate and *trans*-methyl cinnamate, these have been calculated for both *s-cis* and *s-trans* conformations. The computed values for *s-trans* conformer are nearer to the experimental values. Theoretical calculations indicate that the methylene protons in dimethyl methylene malonate (**4**) would be deshielded to δ 7.535 and δ 7.488 ppm compared to methyl acrylate. Due to the introduction of a phenyl group in dimethyl benzylidenemalonate the computed value of the alkene proton is further deshielded and it moves to a lower field of δ 8.028; the observed value being δ 7.92.

Global and local reactivity indices – Analysis of 1,3-dipolar cycloaddition reactions of *C*-phenyl-*N*-methyl nitrones to α,β -unsaturated ester dipolarophiles

The selectivities of 1,3-dipolar cycloaddition reactions of nitrones have been recently analyzed in terms of DFT based reactivity indices by a number of leading research groups²³. This approach has been found to be more reliable than the frontier molecular orbital theory^{20,21}. Chattaraj *et al.*²⁴ have reviewed the utility of the concept of electrophilicity index and its various extensions. The

Table 3. Theoretical and experimental wave numbers (in cm^{-1}) of (**5**)

Theoretical (calculated with scaling) description	Experimental ^a	Approx.
3089	3106	$\alpha(\text{C-H}) \pi$
3063	3071(w)	$\beta(\text{C-H}) \pi$
3053		$\beta(\text{C-H}) \pi$
3034	3033(w)	1, $\beta(\text{C-H}) \Delta$
3020	2990	2, $\beta(\text{C-H}) \Delta$
2929	2950(w)	1, $\alpha(\text{C-H}) \Delta$
2922	2848(w)	2, $\alpha(\text{C-H}) \Delta$
1724	1724(s)	1, $\beta(\text{C-O})$
1697	1685(m)	2, $\alpha(\text{C-O})$
	1636(m)	
1592	1622(m)	$(\text{C-H}) \gamma + 4(\text{C-H}) \pi, \gamma + \Delta (\text{CH}_3) \omega + \alpha (\text{C=C})$
1571	1577(w)	$2\alpha(\text{C=C}) \pi + 4(\text{C-H}) \pi, \gamma + 2\phi (\text{C-H}) \Delta$
1437	1432(s)	$\Delta (\text{CH}_3) \psi$
1410	1406(w)	$\Delta (\text{CH}_3) \psi$
1310	1320(m)	2, $\alpha(\text{C-H}) \Delta$
1280	1270(m)	5(C-H) π, γ
1219	1222(s)	$\alpha(\text{C=C}) \pi + \alpha (\text{C-C})$
1190	1202(s)	4, $\gamma(\text{C-H}) \pi + \delta (\text{C-H})$
	1183(m)	
1163	1156(m)	$\delta(\text{C-H}) + \delta(\text{C=C}) \pi$
1119	1109(w)	$\alpha(\text{C-H}) \pi + \alpha(\text{C-C})$
1051	1066(s)	3(C-H) π, γ
1009	1027(w)	$\Delta (\text{CH}_3) \omega$
996	1001(w)	$\Delta (\text{CH}_3) \omega + 4(\text{C-H}) \pi, \gamma$
973	976(m)	$\delta(\text{H-C-C}) \pi$
967	952(m)	$\delta(\text{H-C-C}) \pi + \Delta (\text{CH}_3) \omega$
943	935(m)	$\gamma(\text{C-H}) \pi + \Delta (\text{CH}_3) \omega$
897	899(m)	$\delta(\text{C-C-C}) \pi$
820	833(m)	4(C-H) π, γ
	805(m)	
781	768(s)	4(C-H) π, ψ

Table-3 (contd.)

723	721(m) 693(s)	$\phi(\text{C-C-C}) \pi$
637	623(m)	4(C-H) π , δ
597	608(m) 580(m)	$\delta(\text{C-C-C}) \pi + \delta(\text{CH}_3) \Delta$
539	539(m)	$\gamma(\text{C-C-C}) \pi$
483	488(w)	$\tau(\text{O-C-C-C}) + \tau(\text{H-C-C-C}) + \tau(\text{C-C-C-C})$
408	406(m)	$\tau(\text{O-C-C-C}) + \tau(\text{H-C-C-C}) + \tau(\text{C-C-C-C})$
394		$\tau(\text{H-C-C-C}) + \tau(\text{C-C-C-C}) + \tau(\text{O-C-C-C})$
180		$\delta(\text{C-O}) + \Delta(\text{CH}_3) \psi$
165		$\delta(\text{C-O}) + \Delta(\text{CH}_3) \psi$
136		$\alpha(\text{C-H}) \Delta$
118		$r(\text{C-C-C-O})$
104		$\alpha(\text{C-H}) \Delta$

^as = strong; w = weak; m = medium, ^b α = symmetric stretching, β = antisymmetric stretching, γ = in-plane bending, δ = out-of-plane bending, ϕ = symmetric bending, ψ = asymmetric bending, Δ = CH₃, τ = torsion, π = phenyl, ω = antisymmetric bending, r = rocking.

Table 4. Experimentally recorded and DFT/B3LYP/6-311 + +G(d,p) calculated GIAO nuclear magnetic shielding tensors of dipolarophiles (1-5) (relative to TMS in ppm)

Methyl acrylate											
a	=CH ₍₃₎	=CH ₍₄₎	=CH ₍₆₎	CH ₃							
b	6.40	5.82	6.13	3.76							
c	1a	6.524	6.045	6.133	H ₁₀	H ₁₁	H ₁₂				
					3.702	3.507	3.720				
	1b	6.841	5.884	6.302	H ₁₀	H ₁₁	H ₁₂				
					3.44	3.726	3.724				
<i>trans</i> -Methyl cinnamate											
a	=CH ₍₁₄₎	=CH ₍₁₆₎	Me				Ph				
b	7.70	6.45	3.81				7.29-7.64				
c	3a	8.001	6.610	H ₂₀	H ₂₁	H ₂₂	H ₇	H ₈	H ₁₀	H ₁₁	H ₁₂
				3.761	3.473	3.761	7.443	8.001	7.443	7.443	7.443
	3b	=CH ₍₁₄₎	=CH ₍₁₆₎	H ₂₀	H ₂₁	H ₂₂	H ₇	H ₈	H ₁₀	H ₁₁	H ₁₂
		7.824	6.483	3.520	3.763	3.763	7.467	7.973	7.467	7.467	7.467
Dimethyl methylene malonate (4)											
a	-CH ₂ -	-OCH ₃									
		H _{(13),(16)}	H _{(14),(15),(17),(18)}								
c	7.535	3.605	3.784 (3.755 and 3.262)								
	7.488										
Dimethyl benzylidene malonate (5)											
a	=CH ₍₁₃₎	Aromatic =CH- protons				-OCH ₃					
d	7.92	7.48-7.58				3.96					
		H _{(8),(11),(12)}	H ₍₁₀₎	H ₍₇₎	H _{(23),(25),(26)}	H _{(27),(28)}	H ₍₂₄₎				
c	8.028	7.476	8.294	7.593	3.578	3.781	3.293				

a : Numbering according to figures; b : Experimental ¹H NMR chemical shifts relative to TMS from spectral data base¹⁵; c : DFT/B3LYP[6-311 + +G(d,p)] calculated nuclear magnetic shielding tensors (relative to TMS) in ppm of the respective protons; d : Experimentally recorded ¹H NMR chemical shifts relative to TMS, recorded during present work.

basic theoretical concepts which have been applied in our analysis of 1,3-DCs are well-established. Hence a detailed presentation of these have not been made; only the equations have been given and the relevant papers cited^{24c,25}.

The electronic chemical potential μ ²⁶ is the negative of electronegativity; it is the index pointing to the direction of the electronic flux during a reaction, i.e. the charge transfer (CT) within the system in its ground state. Chemical hardness η ²⁷ gives the resistance to the charge transfer process. Parr introduced the concept of chemical hardness. The chemical hardness is considered to be a measure of the stability of a system; the most stable system having the maximum hardness²⁷. These quantities may be expressed in terms of one-electron energies of the HOMO and LUMO, ϵ_H and ϵ_L respectively using Koopman's theorem²⁸ :

$$\mu \approx (\epsilon_H + \epsilon_L)/2 \text{ and } \eta \approx (\epsilon_L - \epsilon_H)$$

Global softness S is given by the inverse of 2η ²⁷.

The Fukui functions²⁹ of an atom in a molecule have proved to be useful criteria to characterise the reactive sites within a chemical species. The Fukui functions f_k^+ and f_k^- at the k -th atom is given by the following expressions :

$$f_k^+ = q_k(N + 1) - q_k(N); \text{ for nucleophilic attack}$$

$$f_k^- = q_k(N) - q_k(N - 1); \text{ for electrophilic attack}$$

where $q_k(N + 1)$, $q_k(N)$, $q_k(N - 1)$ represents the respective electron populations of the cationic, neutral and anionic systems on the k -th atom. A high value of the Fukui function implies a high reactivity of the site.

The global electrophilicity index^{23a,23b,24a,24b}, ω , measures the stabilization in energy when a system acquires an additional electronic charge, ΔN , from the environment. It is expressed by $\omega = \mu^2/2\eta$. The global electro-

philicity index (ω) includes the propensity of the electrophile to acquire an additional electronic charge as well as the resistance to exchange the electronic charge with the environment simultaneously.

The local electrophilicity index^{24c,30-32} ω_k is expressed as $\omega_k = \omega_k^+ = \omega f_k^+$.

The electronic chemical potential μ , the chemical hardness η , global softness S and global electrophilicity index ω of the dipolarophiles (**1-5**) and nitrene (**6**) have been calculated at the B3LYP/6-311++G(d,p) level are given in Table 5. These have been used to predict the regioselectivity of cycloadditions to in this communication.

Sustmann and Trill had classified³³ 1,3-dipolar cycloadditions into three types with respect to the 1,3-dipolar species (HOMO controlled, HOMO-LUMO controlled and LUMO controlled) depending on the relative disposition of the frontier orbitals, leading to further simplification. The results of the present work – DFT/B3LYP/6-311++G(d,p) calculated FMO energies along with the HOMO and LUMO surfaces of the dipolarophiles (**1-5**) and nitrene (**6**) have been provided in Fig. 3. The Frontier orbital energy gaps for the cycloaddition reactions of (**6**) to the dipolarophiles (**1-5**) have been listed in Table 6. In all cases, the $\text{HOMO}_{\text{Dipolarophile}} - \text{LUMO}_{\text{Dipole}}$ gaps are smaller than the $\text{HOMO}_{\text{Dipole}} - \text{LUMO}_{\text{Dipolarophile}}$ interaction. Hence the former will be the predominant interaction in each case, this reveals normal electron demand (NED) character of these cycloaddition reactions – Sustmann Type I³³ – also termed as HOMO-dipole controlled reactions. The differences between $\{(\text{LUMO}_{\text{Dipole}} - \text{HOMO}_{\text{Dipolarophile}}) - (\text{LUMO}_{\text{Dipolarophile}} - \text{HOMO}_{\text{Dipole}})\}$ vary significantly (Table 6), but not enough to affect the overall nature of the process as NED cy-

Table 5. DFT/B3LYP/6-311G++(d,p) computed electronic chemical potential μ , chemical hardness η , chemical softness S and global electrophilicity indices ω of dipolarophiles (**1-5**) and nitrene (**6**)

Global properties	Methyl acrylate (1a)	<i>cis</i> -Methyl cinnamate (2b)	<i>trans</i> -Methyl cinnamate (3a)	Dimethyl methylene malonate (4)	Dimethyl benzylidene malonate (5)	<i>C</i> -Phenyl- <i>N</i> -methyl nitrene (6)
μ	-0.158	-0.161	-0.163	-0.177	-0.171	-0.141
η	0.226	0.177	0.169	0.204	0.165	0.154
S	2.213	2.826	2.962	2.451	3.030	3.247
ω	0.0553	0.0732	0.0786	0.0761	0.0894	0.0645

cloadditions. The $\text{HOMO}_{\text{Dipole}} - \text{LUMO}_{\text{Dipolarophile}}$ energy gap decreases in the order methyl acrylate (**1**) > methyl cinnamate (**2-3**) > (**4**) > dimethyl malonate (**5**). The energy gap between the FMOs is less for the nitronc cycloaddition of malonate (**5**) compared with the methyl cinnamates this implies greater reactivity of the former, in conformity with experimental results.

The electronic chemical potential of nitronc (**6**) is higher than that of the dipolarophiles. This also indicates a normal electron demand for reactions of (**2-5**) with (**6**). The global electrophilicity indices of the dipolarophiles are for the most part slightly higher than that of nitronc (**6**), except for the methyl acrylate.

Theoretical analyses of the cycloadditions of *C*-phenyl-*N*-methyl nitronc, and several *C*-hetaryl-*N*-methyl nitroncs, to methyl acrylate has been reported by Merino *et al.*^{9b}, who calculated the transition state energies and geometries at B3LYP/6-31G(d) level of theory. His analysis of relative electronic (ΔE) and free energies (ΔG) of reactants and ground states shows that, in general, *endo* attacks (leading to *trans* adducts) are preferred to the corresponding *exo* approaches (leading to *cis* adducts). Further, there is not a clear preference between the alternative regioisomeric channels, thus predicting that mix-

tures of 3,5- and 3,4-adducts will be obtained. This situation is particularly manifest for nitronc (**6**) and methyl acrylate and for which $\Delta\Delta G$ 0.68 kcal/mole for the alternative transition states was computed, favouring the 3,4-*trans* structure; calculated $\Delta\Delta E$ for these favored the 3,5-*trans* structure by 0.85 kcal/mole.

In view of Merino's paper^{9b}, we have confined our analysis to the 1,3-dipolar cycloadditions of nitronc (**6**) to dipolarophiles (**2-5**) only.

Theoretical analysis of the regioselectivities of 1,3-dipolar cycloaddition reactions of nitroncs have been reported in terms of local electrophilicity index ω_k and the condensed Fukui function for electrophilic attack f_k^- ²⁹. Aurell *et al.*³⁴ reported the theoretical study on the regioselectivity of 1,3-dipolar cycloaddition reactions using DFT based reactivity indices. The report summarized that the regioselectivity can be consistently explained by the most favorable interactions between the highest nucleophilic and electrophilic sites of the reagents. We have recently rationalized⁷ the experimentally observed regioselectivities of the cycloaddition reactions of 1-pyrroline-1-oxide with methyl cinnamate and benzylidene acetone by means of local electrophilicity indices and condensed Fukui functions of the reactants. The condensed

Table 6. Computed energy differences between the two possible HOMO/LUMO interactions for the dipole and the dipolarophiles (values in a.u., eV)

Reaction	$E_{\text{LUMO}}^{\text{Dipolarophile}} - E_{\text{HOMO}}^{\text{Dipole}}$		$E_{\text{LUMO}}^{\text{Dipole}} - E_{\text{HOMO}}^{\text{Dipolarophile}}$		$(E_{\text{LUMO}}^{\text{Dipole}} - E_{\text{HOMO}}^{\text{Dipolarophile}}) - (E_{\text{LUMO}}^{\text{Dipolarophile}} - E_{\text{HOMO}}^{\text{Dipole}})$	
	in a.u.	in eV	in a.u.	in eV	in a.u.	in eV
Nitronc (6) + methyl acrylate (1)	0.155	4.218	0.225	6.122	0.070	1.905
Nitronc (6) + <i>cis</i> -methyl cinnamate (2a)	0.146	3.973	0.185	5.034	0.039	1.061
Nitronc (6) + <i>cis</i> -methyl cinnamate (2b)	0.138	3.755	0.185	5.034	0.047	1.279
Nitronc (6) + <i>trans</i> -methyl cinnamate (3a)	0.139	3.782	0.184	5.007	0.045	1.224
Nitronc (6) + <i>trans</i> -methyl cinnamate (3b)	0.139	3.782	0.183	4.979	0.044	1.197
Nitronc (6) + dimethyl methylenemalonate (4)	0.143	3.891	0.215	5.850	0.072	1.959
Nitronc (6) + dimethyl benzylidenemalonate (5)	0.130	3.537	0.189	5.143	0.059	1.605

Fukui functions f_k^+ , f_k^- and the local electrophilicity indices ω_k for the olefinic carbons of the dipolarophiles, and that for the oxygen and carbon ends of the nitron functionality are given in Table 7.

Table 7. DFT/B3LYP/6-311 + +G(d,p) calculated, electrophilic and nucleophilic Fukui functions of dipolarophiles (2-5) and nitron (6), k is the site at which the property is being evaluated according to Fig. 4

	f_k^+	ω_k^+	f_k^-
<i>cis</i> -Methyl cinnamate (2b)			
C9 (C- β)	0.156	0.0114	0.102
C13 (C- α)	0.111	0.0081	0.105
<i>trans</i> -Methyl cinnamate (3a)			
C9 (C- β)	0.131	0.0103	0.060
C13 (C- α)	0.129	0.0101	0.071
Dimethyl methylenemalonate (4)			
C1 (C- β)	0.326	0.0248	0.128
C2 (C- α)	0.105	0.0079	0.149
Dimethyl benzylidenemalonate (5)			
C9 (C- β)	0.148	0.0132	0.140
C14 (C- α)	0.111	0.0099	0.187
Electrophilic and nucleophilic Fukui indices for the O and C atoms of the nitron (6)			
Atoms	f_k^+	ω_k^+	f_k^-
O15	0.135	0.0087	0.296
C9	0.090	0.0058	0.156

In case of the dipolarophiles (2, 4, 5), C β has the higher local electrophilicity index ω_k than that of C α – where C α refers to the olefinic carbon attached to the carbomethoxy group. For dipole (6), oxygen atom has higher f_k^- compared to the carbon atom. Therefore the preferred two center interaction will take place between the oxygen atom of the dipoles and C β of the dipolarophiles. This predicts the generation of 4-carbomethoxy substituted isoxazolidines from these cycloaddition reactions. The preference will be minimal for (3), as both C α and C β have similar ω_k . In this case the less important charge transfer interaction, viz. from dipolarophile (3) to nitron (6) will also determine the regiochemical outcome; the preferred two center interaction is between is on the nitron oxygen (larger ω_k^+) with C α (higher f_k^-) (3) – thus leading to the 4-carbomethoxy isoxazolidine cycloadduct.

Conclusion

Density functional theory calculations have been carried out to determine the optimized molecular geometries, Frontier orbital energies, the thermodynamic parameters, vibrational frequencies and ^1H NMR chemical shifts of different α,β -unsaturated ester dipolarophiles nitron and compared with the experimental values. The selectivities for the 1,3-DC reactions of C-phenyl-N-methyl nitron with different dipolarophiles have been predicted using DFT reactivity indices. The calculated reactivity indices have been used to analyse reactivities and predict regioselectivities of these unsaturated esters as dipolarophiles with C-phenyl-N-methylnitron

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