Computational Studies of 1,3-Dipolar [3 + 2]-Cycloaddition Reactions of Fullerene-C\textsubscript{60} with Nitrones

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Abstract

Solubility of fullerene-C\textsubscript{60} improves with functionalization. 1,3-dipolar [3+2]-cycloaddition reactions of fullerene-C\textsubscript{60} with substituted nitrones, a versatile method for fullerene functionalization, were investigated at the M06/6-31G*/PM3 level of theory to elucidate the effect of electron-releasing (-CH\textsubscript{3}, -CH\textsubscript{2}CH\textsubscript{3}, -CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}, C\textsubscript{6}H\textsubscript{5}CH\textsubscript{2}) substituents and electron-withdrawing substituents (-F, -Cl, -Br, -NC, and -NO\textsubscript{2}) on the energetics of the reaction; the regio- and stereo-selectivity of the mono- and bis-addition of nitrones; and global reactivity descriptors of the molecular systems to rationalize and predict their chemical reactivity and site selectivity. The results show that electron-withdrawing groups on the nitrones increase the activation barrier of the reaction whereas electron-donating groups decrease the activation barriers. However, electron-withdrawing groups on the nitrones result in more stable products compared to the electron-donating groups. It was found that the reactions with electron-donating substituents on the nitron are normal electron demand reactions, with C\textsubscript{60} as the dipolarophile and the substituted nitrones as the dipoles while the reactions with electron-withdrawing substituents on the nitrones are inverse electron demand reactions. The chemical hardness values show greater positive values for adducts with electron-withdrawing substituents on the nitrone and smaller negative values for adducts with electron-donating substituents on the nitrone, confirming the trend that larger activation barriers accompany reactions with electron-withdrawing substituents on the nitrone while electron-donating substituents lower activation barriers. The activation barriers of the second nitrone addition (bisadduct formation) were found to be lower than the barriers for the first nitrone addition (monoaadduct formation). Stereo-chemically, syn-bisaddition was found to be thermodynamically and kinetically stable favored over anti-bisaddition. Electron donating and electron-withdrawing substituents have a marked effect on the energetics of the reaction.

Keywords: Fullerenes; Functionalization; Cycloaddition; Computational

Introduction

Over the past decades, the field of fullerene chemistry has developed remarkably, driven by the structural novelty and the intriguing properties of fullerenes that offer a wide variety of new possibilities in a diverse range of applications. Since the initial discovery of the fullerene C\textsubscript{60} [1] and the development of a method for its preparation [2], fullerene-based complex molecular systems have received great attention [3-5]. Fullerene-C\textsubscript{60} has many potential applications such as in synthetic chemistry, artificial photosynthesis, non-linear optics, surface coatings, superconductivity devices, and cosmetics to slow down the aging of the human skin. The high capability of C\textsubscript{60} to act as an electron acceptor or even as electron accumulator has led to the synthesis of a large number of compounds in which the fullerene is covalently linked to photoactive groups serving as potential electron donors [6]. The size, hydrophobicity, three-dimensionality and electronic configurations of fullerenes make them an appealing subject in medicinal chemistry. For example, fullerene C\textsubscript{60} is interesting photo, electrochemical and physical properties, which can be exploited in various medical fields. Fullerenes are able to fit inside the hydrophobic cavity of HIV-proteases, inhibiting access of substrates to the catalytic site of enzymes [7]. A series of fullerene-C\textsubscript{60} derivatives displays a wide range of biological properties, including neuroprotective, enzymatic, antiapoptotic, antibacterial, DNA photocleaving [8], nitric oxide synthase inhibiting, and chemotactic activities. Moreover, C\textsubscript{60} is able to efficiently generate cytotoxic singlet oxygen due to a practically unity value of intersystem crossing from the singlet excited state to the first excited triplet state [9]. It can be used as radical scavenger and antioxidant [10]. Water-soluble fullerenes have been investigated as neuroprotective agents, HIV protease inhibitors, MRI contrast agents, etc. [11]. It has been established that C\textsubscript{60} can be used as a versatile building block for the construction of globular dendrimers [12]. Furthermore, an antibody or an antibody fragment can be linked to the fullerene molecule, based on which the C\textsubscript{60} can be used as an efficient multiplier in modular drug delivery systems for a photodynamic therapy of tumors [13]. In such systems the antibody linked to the fullerene acts as a selective addressing unit. Special dye molecules which become cytotoxic after illumination with certain wavelength due to singlet oxygen generation which are attached to the C\textsubscript{60} directly or via dendritic structure are used as photosensitizers [13,14]. Because fullerene-C\textsubscript{60} has a unique spherical geometry, it constitutes a singular scenario in a variety of chemical reactions in which the highly reactive double bonds (30 for the most common C\textsubscript{60}) partake actively. Even though fullerenes have been among the most studied molecules in science over the last two decades since its preparation in multigram amounts, many important reactions in the arsenal of organic chemistry have not been extensively applied to fullerenes synthetically, despite the unprecedented chemical structures that could be formed.

The structure of C\textsubscript{60} includes two different types of bonds, those at the junction of two hexagons and those at the junction of a pentagon and a hexagon (Scheme 1). A pentagon in C\textsubscript{60} is surrounded by five hexagons thereby forming [5,6] C-C junctions and also [6,6] C-C junctions between the neighbouring hexagons. The mean [5,6] C-C
been developed for the functionalization of C_{60}, the main ones being
atoms in the organic addend have been prepared, for example, the C_{60}-
fullerene derivatives containing nitrogen and oxygen
from the reaction between an aldehyde or ketone and an amino acid
dipole moment. In fact, C_{60} is almost completely insoluble in protic or
organic solvents, which decreases substantially their processibility
polyene [16,17]. The major drawback of fullerenes is their low solubility
fullerene-C_{60} improves with functionalization. Many reactions have
with the solubility increasing from pentane to decane. Solubility of
C_{60} derivatives [21]. The azomethine ylide is generally formed
out as the most frequently applied reaction in the preparation of
[3+2] cycloaddition
that reacts further into a cyclopropanated C_{60} derivative. The electron
potential and chemical hardness as, \( \omega \approx \mu^2/2\eta \) where \( \mu \approx – (I + A)/2 \)
are the electronic chemical potential and chemical hardness of the
hence their applicability [18]. The solubility of C_{60} has been studied in
[19]. The solvation of C_{60} requires the disruption of many solvent-solvent interactions, which are not
adequately compensated by the interactions between solvent and
C_{60} due to the rigid geometry of the latter and the lack of permanent
dipole moment. In fact, C_{60} is almost completely insoluble in protic or
dipolar aprotic solvents like MeOH, MeCN, tetrahydrofuran (THF),
and Dimethylsulfoxide (DMSO). It is scarcely soluble in alkanes,
with the solubility increasing from pentane to decane. Solubility of
fullerene-C_{60} improves with functionalization. Many reactions have
been developed for the functionalization of C_{60}, the main ones being
cycloadditions and nucleophilic additions [20]. [3+2] cycloaddition
between C_{60} and an azomethine ylide (the Prato reaction) stand
out as the most frequently applied reaction in the preparation of
C_{60} derivatives [21]. The azomethine ylide is generally formed in situ
from the reaction between an aldehyde or ketone and an amino acid
derivative and allows up to five alkyl groups to be introduced to C_{60}
in a one-step reaction. A related reaction that has been frequently used
to prepare C_{60} derivatives is the Bingel reaction [22] in which a halo-
ester or ketone is first deprotonated by a base and subsequently added
to one of the double bonds in C_{60} resulting in an anionic intermediate
that reacts further into a cyclopropanated C_{60} derivative. The electron
affinity of C_{60} decreases somewhat upon functionalization as a result of
disturbing the conjugated network when converting sp2 carbons into
sp3, an effect that is more pronounced in higher C_{60} adducts. Although
a large number of fullerene derivatives containing nitrogen and oxygen
atoms in the organic addend have been prepared, for example, the C_{60}-
based dyads formed with the well-known electron-donating addends
[23] fullerene derivatives in which the carbon sphere is directly or
otherwise linked to nitrogen and oxygen atoms are among the less
studied modified fullerenes and the mechanism of addition is less
understood. One of the important goals in physical organic chemistry
is to have an appropriate description of the chemical substituents in the
reactivity patterns of molecules. Parr et al. [24,25] have proposed the
global electrophilicity index, \( \omega \) of a molecule in terms of its chemical
potential and chemical hardness as, \( \omega = \mu/2\eta \) where \( \mu = -(I + A)/2 = \left[ E(HOMO + LUMO)/2 \right] \)
and \( \eta = (I - A)/2 = \left[ E(LUMO-HOMO)/2 \right] \)
are the electronic chemical potential and chemical hardness of the
ground state of atoms and molecules respectively, approximated in
terms of the vertical ionization potential (I) and electron affinity (A)
using Koopmans’ theorem. \( \omega \) describes the electrophilic power of a
ligand and also its propensity to soak up electrons. This index measures
the stabilization in energy when the system acquires an additional
electronic charge from the environment. By definition, it encompasses
both the ability of an electrophile to acquire additional electronic
charge and the resistance of the system to exchange electronic charge
with the environment. Global electrophilicity, chemical hardness and
chemical potential are very important global reactivity descriptors
for studying the chemical reactivity and site selectivity of various
molecular systems [26-28]. In view of the above, this work aims at
exploring (1) mono- and bis-1,3-dipolar cycloaddition of nitroene and its
substituted derivatives to fullerene C_{60} (Scheme 2); (2) the effect of
electron-releasing (CH_{3}, CH_{2}, CH_{3}CH_{2}, CH_{3}C_{6}H_{5}CH_{2}) substituents
and electron-withdrawing substituents (F, Cl, Br, NC, and NO_{2}) on
the energetics of the reaction; (3) the regio- and stereo-selectivity of the
mono- and bis-addition and (4) global reactivity descriptors of the
molecular systems to rationalize and predict their chemical reactivity
and site selectivity.

Details of Calculation

All calculations were carried out with the Spartan ‘10 V1.1.0 Molecular
Modeling program (Wavefunction, 2010) at the MO6/6-
31G**/PM3 level of theory. Due to the large size of the systems under
study the geometries could not be fully optimized at higher levels of
theory [29]. The starting geometries of the molecular systems were
constructed using Spartan’s graphical model builder and minimized
interactively using the SYBYL force field [30]. Geometry optimizations
were carried out without symmetry restrictions. A normal mode
analysis was performed to verify the nature of the stationary points.
Equilibrium geometries were characterized by the absence of imaginary
frequencies. Transition state structures were located by a series of
constrained geometry optimizations in which the forming bonds are
fixed at various lengths whiles the remaining internal coordinates were
optimized. The approximate stationary points located from such a
procedure were then fully optimized using the standard transition state
optimization procedure in Spartan. All the critical points were further
characterized by analytical computation of vibrational frequencies.
The transition state structures were found to have only one negative
eigenvalue with the corresponding eigenvector involving the formation
of the newly created C-C and C-O bonds. All reported thermodynamic
and kinetic parameters of interest include thermal corrections at 298.15
K and 1 atmosphere pressure in the gas phase. Only closed-shell singlet
states were considered.

Results and Discussion

Fullerene-C_{60} a polyyne reacts with a typical 1,3-dipole such as
nitrones to yield fullerenoisoxazolidines and substituted derivatives.
As established by Kavitha and Venuvanaligam (2005) in a theoretical
study at the B3LYP/6-31G (d,p)//AM1 level, dipolar cycloaddition
to fullerene - C_{60} can occur at the 6,6 and 6,5 C-C junctions and can
form both open and closed adducts, namely closed 6-6, open 6-6,
closed 6-5 and open 6-5 adducts but among these, the closed 6-6 is the
most favoured. Preliminary calculations in this work to ascertain this
assertion has shown that the closed 6-6 is the most preferred. Therefore, all the calculations reported herein are restricted to closed-shell singlet states at the 6,6 C-C bonds [31].

Substituent effects on the energetics of the reaction

The two types of substituents used are the electron-donating (nucleophilic) and electron-withdrawing (electrophilic) substituents. These substituents are characterized by the presence or absence of electron density in their molecular orbitals. The presence of the electron-donating (ED) and electron-withdrawing (EW) groups defines the direction of flow of electrons between any two or more reacting systems. In the course of a chemical interaction, EW substituents and ED substituents on either the dipole or the dipolarophile affects the transfer of electrons from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) of the reacting species according to frontier molecular orbital (FMO) approximation. The possible substituent positions on the nitronone considered in this work are shown below as R₁, R₂, and R₃. R₁ is on the nitrogen whereas R₂ and R₃ are both on the carbon atom. The reactions involving the various permutations of substituents R₁, R₂, and R₃ are indicated by serial numbers (SN) as given in (Tables 1 and 2).

The effect of electron-donating groups on the energetics

The electron-donating groups considered in this work are H, methyl (CH₃), ethyl (CH₂CH₃), propyl (CH₃CH₂CH₂), pentyl (CH₃CH₂CH₂CH₂CH₃), benzyl (C₆H₅CH₂), and 1-naphthyl (C₁₀H₇) groups. In each reaction, different combination of R₁, R₂, and R₃ are considered. The most feasible [3+2] concerted addition pathway (lowest activation energy) was observed for SN 8 in which R₁ is a propyl group and the other substituents are H atoms, with activation energy of 19.5 kcal/mol. This reaction has an enthalpy of formation of -34.2 kcal/mol. In the stepwise reactions, the activation barriers for the first step are significantly higher than for the second step. The exothermicity of the reactions involving the EW substituents was observed to increase steadily as compared to ED substituents. Analyses of all the stepwise pathways in both cases involving ED substituents and EW substituents show that addition through C-O bond formation first followed by the C-C bond formation is more kinetically favourable than the reverse. Energetics for EW substituents is listed in the (Table 2).

Substituent effect on chemical hardness, chemical potential and global electrophilicity

Table 3 shows the various HOMO-LUMO energy gaps for the adducts

![Scheme 2: 1,3-Dipolar [3 + 2]-Cycloaddition Reaction Of Fullerene-C₆₀ with Nitrones](image)

| SN | R₁    | R₂  | R₃    | ER (kcal/mol) | Eₐ (kcal/mol) |
|----|-------|-----|-------|--------------|--------------|
| 1  | H     | H   | H     | -33.1        | 22.2         |
| 2  | Methyl| H   | H     | -33.1        | 20.3         |
| 3  | Methyl| Methyl| H     | -27.8        | 21.2         |
| 4  | Methyl| Methyl| Methyl| -37.3        | 25.8         |
| 5  | Ethyl | H   | H     | -30.9        | 20.1         |
| 6  | Ethyl | CH₃ | H     | -26.7        | 21.3         |
| 7  | Ethyl | CH₃ | CH₃   | -37.9        | 26.7         |
| 8  | Propyl| H   | H     | -34.2        | 19.5         |
| 9  | Propyl| CH₃ | H     | -27.4        | 9.5, 48.4    |
| 10 | Propyl| CH₃ | CH₃   | -32.4        | 15.8, 26.7   |
| 11 | Propyl| Ethyl| H     | -22.8        | 16.4, 3.8    |
| 12 | Ethyl | Ethyl| Ethyl | -33.6        | 27.0         |
| 13 | Pentyl| Pentyl| Pentyl| -23.7        | 26.7         |
| 14 | Benzyl| H   | H     | -36.4        | 19.8         |
| 15 | Benzyl| Methyl| Methyl| -26.4        | 26.6         |
| 16 | Benzyl| Benzyl| Benzyl| -14.4        | -            |
| 17 | Benzyl| Benzyl| Benzyl| -9.4         | 35.4         |
| 18 | Naphthyl| Benzyl| Benzyl| -8.9         | 37.4         |
| 19 | Naphthyl| Naphthyl| Benzyl| -10.3        | 37.2         |
| 20 | Naphthyl| Naphthyl| Naphthyl| -9.4         | 37.0         |

Table 1: Reaction Energies (Eₐ) and Activation Barriers (Eₐ) of the cycloaddition reactions with the various electron-donating substituents on the nitrones. *Reactions 9, 10, and 11 are stepwise reactions while the rest are concerted. **Barrier of first step in a stepwise mechanism. ***Barrier of second step in a stepwise reaction. All energies are calculated relative to the separated reactants (fullerene+nitrones).
Ele inverse electron demand (IED) values. This means that electron density substituted nitrone is the dipole since NED values are smaller than with EW substituents since their global electrophilicity indices are far higher. Global electrophilicity index (ω). From the calculated energy gaps it is clear that higher electrophilicity is most experienced with ED substituents and other global and local properties such as chemical hardness, <b>ϕ</b> (<eV>), and bis-additions, the C-O is formed in the first step [32]. It is also noteworthy that as the chain of the ED substituents increases, its electrophilic character decreases accordingly. The chemical hardness values (Table 4) show greater positive values for adducts with EW substituents and smaller negative values for adducts with ED substituent. This implies that as the system evolves toward a state of greater hardness, its stability increases. The adduct with the greatest chemical hardness will be the most stable hence least reactive. This conforms perfectly with the activation energies obtained from calculation for both EW and ED systems. Larger activation barriers accompanied EW substituents whereas ED substituents lower the activation barrier.

### Geometrical parameters of transition states and mechanistic pathways

An analyses of the geometries of the transition states associated with these 1,3-dipolar cycloadditions for the various substituents show that most of the concerted reactions follow a synchronous pathway as shown in (Table 5).

### Further addition of nitroto monoadduct (bis-addition)

The addition of nitroto to the cis-1 position of the monoadduct of C60 has two possibilities depending on the orientation of the incoming nitroto. It can be oriented syn or anti to the first nitroto on the buckyball. It is observed that both the syn and anti-additions follow stepwise mechanistic pathways. The syn-addition pathway was found to be kinetically and thermodynamically favoured over the anti-addition pathway. For the syn-pathway, the activation barrier for the first step is 8.3 kcal/mol and that for the second step is 4.2 kcal/mol. The enthalpy of formation of the syn-product is found to be -29.7 kcal/mol as compared to -14.9 kcal/mol for the anti-product which has an activation barrier of 24.2 kcal/mol for the first step and 15.6 kcal/mol for the second step (Figure 1). C-O bond formation in the first steps of both additions is observed to befavoured over the C-C bond formation. The kinetics reveal that formation of the C-O bonds in the first step is about 13.0 kcal/mol favored over the formation of C-C bonds so in both the mono and bis-additions, the C-O is formed in the first step [32].

### Conclusions

The following deductions were made from the results obtained from this work:

1. Electron-withdrawing groups on the nitrones increase the activation

### Table 2: Energetics of the cycloaddition reactions involving electron withdrawing groups

| SN | R1 | R2 | R3 | E1 | E2 |
|----|----|----|----|----|----|
| 21 | -F | -CH3 | -CH3 | 48.7 | 166.3 | -0.1 | -214.4 |
| 22 | -Br | -CH3 | -CH3 | 55.8 | 160.9 | 2.1 | -216.2 |
| 23 | -NC | -CH3 | -CH3 | 48.0 | 167.0 | 2.8 | -214.7 |
| 24 | -Cl | -CH3 | -CH3 | 56.5 | - | -213.1 |
| 25 | -NO2 | -CH3 | -CH3 | 50.7 | - | -216.2 |

* NED: Normal Electron Demand, IED: Inverse Electron Demand, μ: Chemical Potential, ω: Chemical Hardness, υ: Global Electrophilicity Index, DM: Dipole Moment.

### Table 3: HOMO-LUMO energy gap and global and local properties of the adducts with ED substituents

| SN | R1 | R2 | E1 | E2 | μ(eV) | ω(eV) |
|----|----|----|----|----|-------|-------|
| 1  | 6.9 | 9.9 | -6.3 | -3.5 | -5.8 | 3.1 |
| 2  | 6.7 | 9.9 | -6.3 | -3.4 | -5.8 | 2.7 |
| 3  | 8.9 | 9.8 | -7.4 | -4.5 | -6.1 | 2.8 |
| 4  | 6.1 | 9.8 | -5.9 | -3.1 | -5.8 | 3.1 |
| 5  | 6.7 | 9.9 | -6.2 | -3.3 | -5.8 | 2.7 |
| 6  | 6.3 | 9.9 | -6.1 | -3.2 | -5.8 | 2.8 |
| 7  | 6.1 | 9.8 | -5.9 | -3.0 | -5.8 | 3.1 |
| 8  | 6.7 | 9.9 | -6.2 | -3.3 | -5.8 | 2.7 |
| 9  | 6.3 | 9.9 | -6.6 | -3.2 | -5.8 | 3.0 |
| 10 | 6.1 | 9.9 | -5.9 | -3.0 | -5.8 | 3.1 |
| 11 | 6.4 | 9.9 | -6.1 | -3.2 | -5.8 | 2.9 |
| 12 | 6.2 | 9.9 | -6.0 | -3.1 | -5.8 | 3.3 |
| 13 | 6.1 | 9.9 | -6.0 | -3.1 | -5.8 | 2.5 |
| 14 | 6.6 | 8.8 | -6.2 | -3.3 | -5.8 | 2.2 |
| 15 | 6.1 | 9.0 | -6.0 | -3.0 | -5.8 | 2.6 |
| 16 | 6.2 | 9.1 | -6.0 | -3.1 | -5.8 | 2.6 |
| 17 | 6.3 | 9.0 | -6.1 | -3.2 | -5.8 | 2.5 |
| 18 | 6.3 | 8.5 | -6.0 | -3.1 | -5.8 | 2.8 |
| 19 | 6.0 | 8.5 | -6.0 | -3.0 | -5.8 | 2.7 |
| 20 | 5.8 | 8.5 | -5.8 | -2.9 | -5.8 | 2.6 |

### Table 4: Comparison of HOMO-LUMO energy gap and global and local properties of the adducts with electron-withdrawing (EW) and electron-donating (ED) substituents

**Substituent** | **E(LUMO-HOMO)** | **μ(eV)** | **ω(eV)** |
|-------------|-----------------|--------|--------|
| EW          | F               | 15.1   | -8.5   | 1.0    | 35.0 |
| -Br         | 13.1            | -8.5   | 1.0    | 35.8 |
| -NC         | 13.8            | -8.5   | 0.9    | 34.7 |
| -Cl         | 12.6            | -8.4   | 1.0    | 37.0 |
| -NO2        | 14.1            | -8.5   | 0.9    | 33.8 |

**ED**

| Methyl      | 6.1             | -5.9   | -3.1   | -5.8 |
| Ethyl       | 6.1             | -5.9   | -3.0   | -5.8 |
| Propyl      | 6.1             | -5.9   | -3.0   | -5.8 |
| Benzyl      | 6.0             | -5.9   | -3.0   | -5.8 |

* NED: Normal Electron Demand, IED: Inverse Electron Demand, μ: Chemical Potential, ω: Chemical Hardness, υ: Global Electrophilicity Index.
TS: Transition State, i-freq: Imaginary Frequency

Table 5: Optimized C-C and C-O bond lengths of the transition states and products involved in the various reactions.

| SN | C-C (Å) | C-O (Å) | TS C-C (Å) | TS C-O (Å) | i-freq/cm⁻¹ |
|----|---------|---------|------------|------------|-------------|
| 1  | 1.54    | 1.42    | 2.074      | 2.07       | 600         |
| 2  | 1.53    | 1.41    | 2.074      | 2.07       | 603         |
| 3  | 1.55    | 1.41    | 2.103      | 2.10       | 492         |
| 4  | 1.57    | 1.41    | 2.113      | 2.11       | 506         |
| 5  | 1.53    | 1.41    | 2.103      | 2.10       | 524         |
| 6  | 1.55    | 1.41    | 2.103      | 2.10       | 490         |
| 7  | 1.57    | 1.41    | 2.103      | 2.10       | 514         |
| 8  | 1.53    | 1.41    | 2.103      | 2.10       | 526         |
| 12 | 1.55    | 1.42    | 2.103      | 2.10       | 496         |
| 13 | 1.58    | 1.42    | 2.158      | 2.16       | 393         |
| 14 | 1.53    | 1.41    | 2.113      | 2.11       | 486         |
| 15 | 1.57    | 1.41    | 2.113      | 2.11       | 488         |
| 16 | 1.60    | 1.42    | 2.112      | 2.11       | 452         |
| 17 | 1.59    | 1.42    | 2.113      | 2.11       | 442         |
| 18 | 1.59    | 1.42    | 2.113      | 2.11       | 443         |
| 19 | 1.59    | 1.42    | 2.113      | 2.11       | 441         |
| 20 | 1.59    | 1.42    | 2.113      | 2.11       | 441         |

Figure 1: Energy profile diagram comparing the energetics of syn and anti-bisaddition to the monoadduct. All energies are calculated relative to the separated reactants (monoadduct+nitrone).

and smaller negative values for adducts with electron-donating substituents on the nitrene, confirming the trend that larger activation barriers accompany reactions with electron-withdrawing substituents on the nitrene while electron-donating substituents lower activation barriers.

6. The C-O bond formation is favored kinetically over the C-O bond at the saddle point in both the concerted and stepwise mechanistic pathways for all the reactions considered.

References

1. Kroto HW, Heath JR, O’Brien SC, Curl RF, Smalley RE, et al. (1985) C60: Buckminsterfullerene. Nature 318: 162-163.
2. Krätschmer W, Lamb LD, Fostipoulos K, Huffman DR (1990) C60: a new form of carbon. Nature 347: 354-358.
3. Imahori H, Mori Y, Matano Y (2003) Nanostructured artificial photosynthesis. J. Photochem. Photobiol. C 4: 51-83.
4. Osuna S, Morera J, Cases M, Morokuma K, Sola M (2009) Diels-Alder reaction between cyclopentadiene and C60: an analysis of the performance of the ONIOM method for the study of chemical reactivity in fullerenes and nanotubes. J Phys Chem A 113: 9726-9727.
5. Gao XF, Cui CX, Liu JY (2012) Trapping intermediates and comparing relative reactivities: a DFT M06-2X study on Diels–Alder cycloadditions of butadiene to C60. J Phy Org Chem 25: 850-855.
6. Liddell PA, Kodis G, Andréasson J, de la Garza L, Bandyopadhyay S (2004) Photonic switching of photoinduced electron transfer in a dihydrostreptomycin-fullerene molecular triad. J Am Chem Soc 126: 4803-4811.
7. Bakry R, Vallant RM, Najem-ul-Haq M, Rainer M, Szabo Z, et al. (2007) Medicinal applications of fullerenes. Int J Nanomedicine 2: 639-649.
8. Yamakoshi YN, Yagami T, Sueyoshi S, Miyata N (1996) Acrider Adduct of [60] Fullerene with Enhanced DNA-Cleaving Activity. J Org Chem 61: 7236-7237.
9. Krusic PJ, Wasserman E, Keizer PN, Morton JR, Preston KF (1991) Radical reactions of C60. Science 254: 1183-1185.
10. Gharbi N, Pressac M, Hadchouel M, Szwarc H, Wilson SR, et al. (2005) [60] fullerene is a powerful antioxidant in vivo with no acute or subacute toxicity. Nano Lett 5: 2578-2585.
11. Tokuyama H, Nakamura M, Nakamura E (1995) [1 + 2] and [3 + 2] cycloaddition reactions of vinylcarbenes with C60. Tetrahedron Lett 34: 7429-7432.
12. Xavier C, Elke D, Andreas H, Soomi P, Luis E, et al. (1999) Globular dendrimers involving a C60 Core and a tetrapyroleporphyrin function. Chem Eur J 5: 2362-2373.
13. Röder B (2000) Photodynamic therapy in Encyclopaedia Analytical Chemistry. Edited by R. A. Meyers. John Wiley and Sons Ltd: Chichester 302-320.
14. Yamakboshi Y, Umezawa N, Rya A, Arakane K, Miyata N, et al. (2003) Active oxygen species generated from photoexcited fullerene (C60) as potential medicines: O2- versus 1O2. J Am Chem Soc 125: 12803-12809.
15. Taylor R, Watson D (1993) The chemistry of fullerenes. Nature 363: 685-693
16. Ohino M, Koijima S, Shirakawa Y, Eguchi S (1995) Hetero-Diels-Alder reaction of fullerene: Synthesis of thiocyanocarbon-fused C60 with O-thioquinone methide and oxidation to its S-oxides. Tetrahedron Lett 36: 6899-6902.
17. Wang X-B, Ding C-F (1999) High resolution photoelectron spectroscopy of C60-. J Chem Phys 110: 8217-8220.
18. Diederich F (1997) Covalent fullerene chemistry. Pure Appl Chem 69: 395-400.
19. Korobov MV, Allan L (2000) in: Fullerenes; Chemistry, Physics, and Technology, Edited by Kadish, K.M.; Ruoff, R.S. Wiley interscience New York 53.
20. Prato M (1997) [60] Fullerene chemistry for materials science applications. J Mater Chem 7: 1097-1109.
21. Prato M, Maggini M (1998) Fulleropyrrolidines: A Family of Full-Fledged Fullerene Derivatives. Acc Chem Res 31: 519-526.
22. Bingel C (1993) Cyclopropanierung von Fullerenen. Chemische Berichte 126: 1957-1959
23. Martín N (2006) New challenges in fullerene chemistry. Chem Commun (Camb): 2093-2104.
24. Parr RG, Szentpaly LV, Liu S (1999) Electrophilicity index. J Am Chem Soc 121: 1922-1924.
25. Chattaraj PK, Sarkar U, Roy DR (2006) Electrophilicity index. Chem Rev 106: 2065-2091.
26. Elango M, Parthasarathi R, Karthik G, Narayanan A, Sabeelullah MD, et al. (2005) Relationship between Electrophilicity index, Hammett constant and nucleus-independent chemical shift. J Chem Sci 117: 61-65.
27. Meneses L, Fuestealba P, Contreras R (2005) Relationship between the electrophilicity of substituting agents and substrate selectivity in Friedel-Crafts reactions. Tetrahedron 61: 831-836.
28. Castillo R, Andres J (2011) A DFT Study of the Reactivity Indexes of Ionic [4 + 2] Diels-Alder Cycloaddition to Nitrilium and Immonium Ions. Letters in Organic Chemistry 8: 104-107.
29. Spartan (2014) Wavefunction Inc.
30. Cases M, Duran M, Mestres J, Martín N, Solà M (2001) Mechanism of the addition reaction of alkyl azides to [60]fullerene and the subsequent N2 extrusion to form monoimino-[60]fullerenes. J Org Chem 66: 433-442.
31. Clark M, Cramer RD, Opdenbosch NV (1989) Validation of the general purpose tripso 5.2 force field. J Comput Chem 10: 982-1012.
32. Kaviha K, Venuvanalingam P (2005) Open versus closed 1,3-dipolar additions of C60: a theoretical investigation on their mechanism and regioselectivity. J Org Chem 70: 5428-5435.