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*J. Nat. Prod. Plant Resour.*, 2015, 5 (3):18-22
*(http://scholarsresearchlibrary.com/archive.html)*

ISSN : 2231 – 3184
CODEN (USA): JNPPB7

# Understanding the regioselectivity and reactivity of some ethylene compounds using Parr functions

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## ABSTRACT

*A theoretical study of the reactivity and regioselectivity of some ethylene compounds in nucleophilic substitution was carried out using density functional theory with B3LYP/6-31G(d). The relative reactivity of these systems was rationalized by means of the global electrophilicity index. Positional selectivity, namely 1, 2, 3 and 4, was predicted using local electrophilic indices (Parr functions). The present study shows that the experimental results of the relative reactivity and regioselectivity of these reactions is correctly predicted using Parr functions.*

**Key words:** ethylene compounds, regioselectivity, Parr functions, DFT

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## INTRODUCTION

The ethylene compounds represented in Figure 1 show an interesting reactivity [1-3]. These compounds can be considered equivalents of ketene with reversed polarity, with an additional advantage in that halogen substitution by a nucleophilic reagent makes it possible to obtain numerous heterocyclic compounds of therapeutic interest [4-7].

Our aim in this work is to present a theoretical study on the reactions of nucleophilic substitutions. We chose ethylene molecules as substitutes (Figure 1) and compared the results of our calculations with experimental results available in the literature [1-7].

## MATERIALS AND METHODS

Density functional theory (DFT) computations were carried out using DFT/B3LYP [8] exchange-correlation functionals, using the standard 6-31G(d) basis set [9]. Optimization was carried out using the Berny analytical gradient optimization method [10].

All computations were carried out with the Gaussian 09 suite of programs [11]. The global electrophilicity index $\omega$ [12] is given by the expression $\omega=\mu^2/2.\eta$, in terms of electronic chemical potential $\mu$ and chemical hardness $\eta$. Both quantities may be considered in terms of the one-electron energies of the HOMO and LUMO frontier molecular orbitals, as $\varepsilon_{HOMO}$ and $\varepsilon_{LUMO}$, $\mu=(\varepsilon_{HOMO}+\varepsilon_{LUMO})/2$ and $\eta=(\varepsilon_{LUMO}-\varepsilon_{HOMO})$ respectively [13]. We introduced an empirical (relative) nucleophilicity index $N$ [14], based on the HOMO energies obtained within the Kohn–Sham scheme [15] and defined as $N = \varepsilon_{HOMO(Nu)} - \varepsilon_{HOMO(TCE)}$. Nucleophilicity is calculated with reference to tetracyanoethylene (TCE), because this compound presents the lowest HOMO energy of a large series of molecules already investigated in the context of polar cycloadditions, which enables us to handle a nucleophilicity scale of positive values easily.

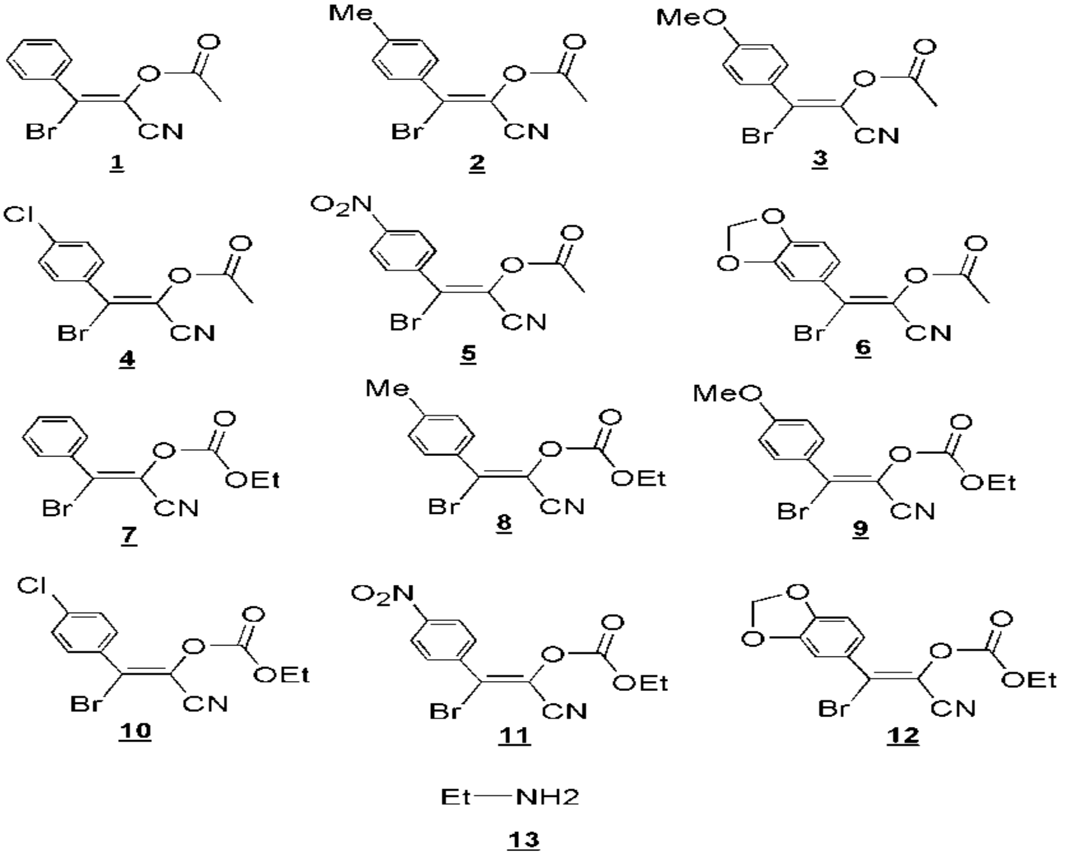

**Figure 1. Ethylene compounds studied in this work**

The $P_k^+$ electrophilic and $P_k^-$ nucleophilic Parr functions [16-24] which enable characterization of the electrophilic and nucleophilic centers of a molecule were obtained by analysis of the Mulliken atomic spin density of the radical anion and the radical cation respectively of the molecules studied.

## RESULTS AND DISCUSSION

### Prediction of relative reactivity

The global indices obtained using DFT are a powerful tool for understanding the behavior of polar reactions. The difference in global electrophilicity between two reactants [25] can be used to predict the polarity of the process and thus the feasibility of these reactions. Tables 1a and 1b show the static global properties: electronic chemical potential $\mu$, global electrophilicity $\omega$, global nucleophilicity $N$, and the difference in global electrophilicity $\Delta\omega$ and global nucleophilicity $\Delta N_{max}$ with regard to the reference value.

**Table 1a. Global reactivity indices $\mu$, $\eta$, $\omega$, $N$, and differences in electrophilicity $\Delta\omega$ and nucleophilicity $\Delta N_{max}$ for the 2-acetoxy-3- bromo prop-2-ene nitriles compounds 1–6 and ethylamine calculated using DFT/B3LYP/6-31G(d)**

| Compound | E/Z | $\mu$ (au) | $\eta$ (au) | $\omega$ (ev) | $N$ (ev) | $\Delta\omega$ (ev) | $\Delta N_{max}$ |
|---|---|---|---|---|---|---|---|
| 1 | E | -0.1671 | 0.1710 | 2.221 | 2.660 | 1.983 | 0.977 |
| | Z | -0.1660 | 0.1626 | 2.306 | 2.804 | 2.068 | 1.021 |
| 2 | E | -0.1622 | 0.1685 | 2.123 | 2.828 | 1.885 | 0.962 |
| | Z | -0.1608 | 0.1591 | 2.212 | 2.990 | 1.974 | 1.011 |
| 3 | E | -0.1545 | 0.1579 | 2.058 | 3.179 | 1.82 | 0.979 |
| | Z | -0.1547 | 0.1642 | 1.982 | 3.089 | 1.744 | 0.942 |
| 4 | E | -0.1696 | 0.1646 | 2.378 | 2.676 | 2.14 | 1.030 |
| | Z | -0.1699 | 0.1802 | 2.180 | 2.457 | 1.942 | 0.943 |
| 5 | E | -0.1920 | 0.1591 | 3.151 | 2.144 | 2.913 | 1.207 |
| | Z | -0.1932 | 0.1722 | 2.949 | 1.932 | 2.711 | 1.122 |
| 6 | E | -0.1597 | 0.1434 | 2.420 | 3.235 | 2.182 | 1.114 |
| | Z | -0.1499 | 0.1551 | 1.972 | 3.342 | 1.734 | 0.967 |
| 13 | | -0.0728 | 0.3037 | 0.238 | 3.419 | - | 0.240 |

*We can deduce from table 1a that:*

- The electronic chemical potential of compound 13 (ethylamine) is greater than that of the ethylene compounds 1-6, which implies that electron transfer takes place from compound 13 to the ethylene compounds 1-6.

- The nucleophilicity index of compound 13 (3.419 eV) is greater than that of the six ethylene compounds, implying that in this substitution compound 13 behaves as a nucleophile while the six ethylene compounds (E and Z) behave as electrophiles.

- The global electrophilic indices of the reactants confirm that compound 13 is a nucleophile and the six ethylene compounds are electrophiles.

We can also deduce from table 1b that:

- The electronic chemical potential of compound 13 (ethylamine) is higher than that of compounds 7-12, which implies that the transfer of electrons takes place from compound 13 to compounds 7-12.

- The nucleophilicity index of compound 13 (ethylamine) is higher than that of products 7-12, implying that in this reaction compound 13 behaves as a nucleophile while compounds 7-12 behave as electrophiles.

The difference between the global electrophilicity index and the reference is greater than 1 eV for all compounds ($\Delta\omega$>1 eV), showing that this reaction has low polarity.

**Table 1b. Global reactivity indices $\mu$, $\eta$, $\omega$, $N$, and differences in electrophilicity $\Delta\omega$ and nucleophilicity $\Delta N_{max}$ for the ethyl carbonate compounds 7–12 and ethyl amine 13 calculated using DFT/B3LYP/6-31G(d)**

| Compound | E/Z | $\mu$ (au) | $\eta$ (au) | $\omega$ (ev) | $N$ (ev) | $\Delta\omega$ (ev) | $\Delta N_{max}$ |
|---|---|---|---|---|---|---|---|
| **7** | E | -0.1629 | 0.1747 | 2.068 | 2.722 | 1.83 | 0.933 |
| | Z | -0.1655 | 0.1982 | 1.881 | 2.332 | 1.643 | 0.835 |
| **8** | E | -0.1578 | 0.1703 | 1.988 | 2.923 | 1.75 | 0.926 |
| | Z | -0.1587 | 0.1889 | 1.815 | 2.642 | 1.577 | 0.840 |
| **9** | E | -0.1503 | 0.1611 | 1.909 | 3.251 | 1.671 | 0.933 |
| | Z | -0.1490 | 0.1698 | 1.779 | 3.167 | 1.541 | 0.878 |
| **10** | E | -0.1679 | 0.1700 | 2.256 | 2.651 | 2.018 | 0.988 |
| | Z | -0.1652 | 0.1876 | 1.979 | 2.486 | 1.741 | 0.881 |
| **11** | E | -0.1890 | 0.1616 | 3.006 | 2.192 | 2.768 | 1.169 |
| | Z | -0.1858 | 0.1646 | 2.853 | 2.238 | 2.615 | 1.129 |
| **12** | E | -0.1543 | 0.1477 | 2.195 | 3.324 | 1.957 | 1.045 |
| | Z | -0.1526 | 0.1528 | 2.073 | 3.303 | 1.835 | 0.999 |
| **13** | | -0.0728 | 0.3037 | 0.238 | 3.419 | - | 0.240 |

### Prediction of the regioselectivity of the reaction using local electrophilicity indices

According to the polar model proposed by Chattaraj [26], the local philicity indices ($\omega_k$ and $N_k$) are reliable indicators for predicting the most favored interaction between two polar centers. The most favored regioisomer is that which is associated with the highest local electrophilicity index $\omega_k$ of the electrophile and the highest local nucleophilicity index $N_k$ of the nucleophile. We determined $N_k$ for aromatic compounds 1-12 in order to predict the most likely electrophile/nucleophile interaction throughout the reaction pathway, and so elucidate the regioselectivity of these reactions.

Table 2 presents local electrophilicity $\omega_k$ in positions 1, 2, 3 and 4 of compounds 1-12.

Analysis of local electrophilicity of the compounds indicates that the $C_1$(Br) carbon is the most electrophilic in all compounds except for compounds 5 and 11, where $C_2$ is the most electrophilic. Consequently, the most favorable regioisomeric channels involved in these reactions are those in which there is initial formation of a N–C(Br) bond. Regioselectivity is correctly predicted by the Parr function.

**Table 2. Local electrophilicity $\omega_k$ in positions 1, 2, 3 and 4 of the acetoxy-2 bromo-3 propene compounds 1–6 and ethyl carbonate compounds 7–12**

| **Compound** | | **$C_1$(Br)** | **$C_2$** | **$C_3$(-N)** | **$C_4$(=O)** |
|---|---|---|---|---|---|
| **1** | E | 0.767 | 0.428 | 0.040 | 0.017 |
| | Z | 0.735 | 0.491 | -0.042 | 0.037 |
| **2** | E | 0.692 | 0.449 | -0.037 | 0.035 |
| | Z | 0.778 | 0.418 | 0.045 | 0.017 |
| **3** | E | 0.691 | 0.437 | -0.035 | 0.034 |
| | Z | 0.684 | 0.380 | 0.037 | 0.143 |
| **4** | E | 0.692 | 0.506 | -0.049 | 0.037 |
| | Z | 0.793 | 0.362 | -0.014 | 0.013 |
| **5** | E | 0.486 | 0.511 | -0.066 | 0.033 |
| | Z | 0.493 | 0.259 | -0.021 | 0.003 |
| **6** | E | 0.811 | 0.516 | -0.041 | 0.037 |
| | Z | 0.809 | 0.357 | -0.009 | 0.015 |
| **7** | E | 0.647 | 0.452 | -0.045 | 0.027 |
| | Z | 0.447 | 0.176 | -0.003 | 0.007 |
| **8** | E | 0.619 | 0.431 | -0.043 | 0.025 |
| | Z | 0.837 | 0.327 | -0.006 | 0.012 |
| **9** | E | 0.631 | 0.418 | -0.040 | 0.025 |
| | Z | 0.746 | 0.338 | -0.012 | 0.011 |
| **10** | E | 0.632 | 0.496 | -0.057 | 0.027 |
| | Z | 0.606 | 0.477 | -0.040 | 0.046 |
| **11** | E | 0.415 | 0.483 | -0.068 | 0.022 |
| | Z | 0.324 | 0.609 | -0.053 | 0.005 |
| **12** | E | 0.700 | 0.491 | -0.054 | 0.037 |
| | Z | 0.591 | 0.539 | -0.009 | -0.004 |

## CONCLUSION

In this work, we carried out a theoretical examination of the reaction of a series of ethylene compounds with ethylamine in nucleophilic substitution. Our calculations show that experimental regioselectivity is correctly reproduced. The local electrophilicity index shows that the $C_1$(Br) atom is the most electrophilic in all the compounds studied, except in compounds 5 and 11: in these last two, which both include a nitrobenzene cycle, the $C_2$ atom is the most electrophilic. We can therefore conclude that local electrophilicity as defined by Domingo's group using the Parr function can adequately predict regioselectivity in nucleophilic substitution.

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