The Cis-Effect Explained Using Next-Generation QTAIM

Yuting Peng 1, Wenjing Yu 1, Xinxin Feng 1, Tianlv Xu 1, Herbert Früchtl 2, Tanja van Mourik 2, Steven R. Kirk 1,∗ and Samantha Jenkins 1,∗

1 Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research and Key Laboratory of Resource National and Local Joint Engineering Laboratory for New Petro-chemical Materials and Fine Utilization of Resources, College of Chemistry and Chemical Engineering, Hunan Normal University, Changsha 410081, China
2 EaStCHEM School of Chemistry, University of St Andrews, North Haugh, St Andrews, Fife KY16 9ST, Scotland, UK
∗ Correspondence: steven.kirk@cantab.net (S.R.K.); samanthajsuman@gmail.com (S.J.)

Abstract: We used next-generation QTAIM (NG-QTAIM) to explain the cis-effect for two families of molecules: C2X2 (X = H, F, Cl) and N2X2 (X = H, F, Cl). We explained why the cis-effect is the exception rather than the rule. This was undertaken by tracking the motion of the bond critical point (BCP) of the stress tensor trajectories Tσ(s) used to sample the Uσ-space cis- and trans-characteristics. The Tσ(s) were constructed by subjecting the C1-C2 BCP and N1-N2 BCP to torsions ±θ and summing all possible Tσ(s) from the bonding environment. During this process, care was taken to fully account for multi-reference effects. We associated bond-bending and bond-twisting components of the Tσ(s) with cis- and trans-characteristics, respectively, based on the relative ease of motion of the electronic charge density ρ(rσ). Qualitative agreement is found with existing experimental data and predictions are made where experimental data is not available.

Keywords: QTAIM; NG-QTAIM; cis-effect; dihaloethene; dihalodiazene

1. Introduction

An extensive body of literature exists on the subject of the cis-effect over the last 40 years, on the basis of both theory [1–6] and experiment [6–17]. The cis-effect is a phenomenon in which the cis-isomer is more stable than [2,4,7–9] or, in molecules with double bonds, almost as energetically stable as the corresponding trans-isomer. Computational results of the relative energy differences of the cis- and trans-isomers are compared with existing experimental data [7–16] that in some cases suffer from large uncertainties in the measurements [7,15–17]. In this study, we will not use energy-based approaches to attempt to understand the mechanism of the cis-effect; instead, we will use an electronic charge-density-based analysis.

Earlier, some of the current authors provided a scalar physics-inspired coupling mechanism explaining the cis-effect in terms of electronic and nuclear degrees of freedom for three families of molecules, including halogen-substituted ethene and diazenes [18]. We undertook a static investigation of the properties of the central X = X or N = N bond paths and found that those of the cis-isomers were more bent: the difference between the length of the bond path and the internuclear separation was up to 1.5% larger in the cis-isomers than in the corresponding trans-isomers. In our earlier contribution, we therefore concluded that the physical origin of the cis-effect was associated with greater bond-path bending. This earlier work, however, only provided correlations of the bond-path bending with the energy and did not explain why the cis-effect is the exception rather than the rule. In this work, the physical basis of the cis-effect will be provided in terms of the least and most preferred directions of electronic charge density motion.

Recently, some of the current authors used an electronic charge-density-based analysis to investigate steric effects within the formulation of next-generation Quantum Theory of
Atoms in Molecules (NG-QTAIM) [19]. We found that the presence of chiral contributions suggested that steric effects, rather than hyperconjugation, explained the staggered geometry of ethane [20]. This recent work on steric effects relates to the current investigation on cis-effects, since in both cases we subject the central C = C or N = N bond to a torsion to probe either steric or cis-effects. Low/high values of the NG-QTAIM interpretation of chirality \( C_\sigma \) were associated with low/high steric effects due to the absence/presence of an asymmetry. The chirality \( C_\sigma \) [21] was earlier used to redefine a related quantity for cumulenes, the bond-twist \( T_\sigma \) [22].

In this investigation, we will use NG-QTAIM to explain why the cis-effect was previously found, in our scalar investigation, to be associated with bond bending [18]. This will be undertaken by subjecting the axial bonds, C1-C2 and N1-N2, to a torsion \( \theta \) to sample the directional response of the electronic charge density \( \rho(\mathbf{r}_b) \) at the bond cross-section. This will provide a better understanding of the greater (topological) stability of the cis-isomer over the trans-isomer in these halogen-containing species; see Scheme 1.

Scheme 1. In-plane views of the cis- and trans-isomers for substitutions of the ethene (left panel) and diazene (right panel) molecular graphs, where \( X_3 = X_6 = H, F, Cl \). The atomic numbering scheme of the four substituted ethene isomers for the cis- \( (X_3-C_1-C_2-X_6, X_3-C_1-C_2-H_5, H_4-C_1-C_2-H_5, H_4-C_1-C_2-X_6) \) and trans-isomers \( (X_4-C_1-C_2-X_6, X_4-C_1-C_2-H_5, H_3-C_1-C_2-H_5, H_3-C_1-C_2-X_6) \). The dihedral \( X_3-N_1-N_2-X_4 \) is used for the cis- and trans-isomers of the diazenes. The undecorated green spheres indicate the locations of the bond critical points (BCPs).

2. Theoretical Background and Computational Details

2.1. Theoretical Background

The QTAIM and next-generation QTAIM (NG-QTAIM) [23–29] background is provided in the Supplementary Materials S1, including the procedure to generate the stress tensor trajectories \( T_\sigma(s) \).

We use Bader’s formulation of the quantum stress tensor \( \sigma(\mathbf{r}) \) [30] to characterize the forces on the electron density distribution in open systems that is defined by:

\[
\sigma(\mathbf{r}) = -\frac{1}{4} \left[ \left( \frac{\partial^2}{\partial r_i \partial r'_i} + \frac{\partial^2}{\partial r'_i \partial r_j} - \frac{\partial^2}{\partial r_i \partial r_j} - \frac{\partial^2}{\partial r'_i \partial r'_j} \right) \gamma(\mathbf{r}, \mathbf{r}') \right] \mid_{\mathbf{r}=\mathbf{r}'} ,
\]

(1)

where \( \gamma(\mathbf{r}, \mathbf{r}') \) is the one-body density matrix,

\[
\gamma(\mathbf{r}, \mathbf{r}') = N \int \Psi(\mathbf{r}, \mathbf{r}_2, \ldots, \mathbf{r}_N) \Psi^*(\mathbf{r}', \mathbf{r}_2, \ldots, \mathbf{r}_N) \mathbf{d}r_2 \cdots \mathbf{d}r_N
\]

(2)

The stress tensor is then any quantity \( \sigma(\mathbf{r}) \) that can satisfy equation (2): any divergence-free tensor can be added [30–32]. Bader’s formulation of the stress tensor \( \sigma(\mathbf{r}) \), equation (1), is a standard option in the AIMAll QTAIM package [33]. Earlier Bader’s formulation of \( \sigma(\mathbf{r}) \) demonstrated superior performance compared with the Hessian of \( \rho(\mathbf{r}) \) for distinguishing the \( S_\alpha \) and \( R_\alpha \)-geometric stereoisomers of lactic acid [34] and therefore will be used in this investigation.

In this investigation, we include the entire bonding environment, including all contributions to the \( U_\sigma \)-space cis- and trans-characteristics, by considering the C1-C2 BCP \( T_\sigma(s) \).
of the asymmetric, i.e., ‘reference’ carbon atom (C1) or the N1-N2 BCP $T_\sigma(s)$ of the nitrogen atom (N1); see Scheme 1 and the Computational Details section. The C1-C2 BCP $T_\sigma(s)$ and N1-N2 BCP $T_\sigma(s)$ are created by subjecting these BCP bond paths to a set of torsions $\theta$; see the Computational Details section.

The bond-twist $T_\sigma$ is the difference in the maximum projections, the dot product of the stress tensor $e_1 \sigma$ eigenvector and the BCP displacement $d_r$, of the $T_\sigma(s)$ values between the counter-clockwise (CCW) and clockwise (CW) torsion $\theta$.

$$T_\sigma = [(e_1 \sigma \cdot d_r)_{\text{max}}]_{\text{CCW}} - [(e_1 \sigma \cdot d_r)_{\text{max}}]_{\text{CW}}$$  \hspace{1cm} (3)

Equation (3) for the bond-twist $T_\sigma$ quantifies the bond torsion BCP-induced bond twist for the CCW vs. CW direction, where the largest magnitude stress tensor eigenvalue ($\lambda_{1\sigma}$) is associated with $e_1 \sigma$; see Figures 1 and 2. The eigenvector $e_1 \sigma$ corresponds to the direction along which electrons at the BCP are subject to the most compressive forces. Therefore, $e_1 \sigma$ corresponds to the direction along which the BCP electrons will be displaced most readily when the BCP is subjected to a torsion [35]. Higher values of the bond twist $T_\sigma$ correspond to greater asymmetry, and therefore to a dominance of the trans- compared with the cis-isomer in $U_\sigma$ space. This reflects the structural symmetry, with respect to the positioning of the halogen substituents, of the trans- rather than the cis-isomer.

![Figure 1](image1.png)

**Figure 1.** The torsion C1-C2 BCP stress tensor trajectories $T_\sigma(s)$ for the Cartesian clockwise (CW) and counter-clockwise (CCW) torsion directions for the geometric cis- and trans-isomers of H$_2$-ethene, F$_2$-ethene and Cl$_2$-ethene are presented in sub-figures (a–c), respectively; see Table 1. Notice the markers at 30° intervals.

![Figure 2](image2.png)

**Figure 2.** The N1-N2 BCP stress tensor trajectories $T_\sigma(s)$ for the Cartesian CW and CCW torsions for the cis- and trans-isomers of H$_2$-diazene, F$_2$-diazene and Cl$_2$-diazene are presented in sub-figures (a–c), respectively; see the caption of Figure 1 and Table 2.
Table 1. The U-σ-space bond cross-section sets \( \{T_{σ}, F_{σ}\} \) of the torsion C1-C2 BCP, and the sum \( \sum\{T_{σ}, F_{σ}\} \), of ethene and the cis- and trans-isomers of doubly substituted ethene. The atom numbering sequence for the dihedral angles used to construct the \( T_{σ}(s) \) is indicated by the four-digit sequence (left column); see Scheme 1.

\[
\begin{array}{ccc}
\{T_{σ}, F_{σ}\} & \sum\{T_{σ}, F_{σ}\} \\
H_{2} & & \\
D_{3} & \{−0.00096[R_{σ}], 0.00023[S_{σ}]\} & \{0.01731[R_{σ}], 0.00000[Q_{σ}]\} \\
D_{3} & \{0.00011[R_{σ}], 0.00004[S_{σ}]\} & \{−0.00030[R_{σ}], 0.00028[R_{σ}]\} \\
D_{5} & \{0.00017[S_{σ}], −0.00012[R_{σ}]\} & \{0.00017[S_{σ}], −0.00012[R_{σ}]\} \\
\end{array}
\]

Table 2. The U-σ-space bond cross-section sets \( \{T_{σ}, F_{σ}\} \) of the C1-C2 BCP for the doubly substituted diazene torsion.

\[
\begin{array}{ccc}
\{T_{σ}, F_{σ}\} & \sum\{T_{σ}, F_{σ}\} \\
H_{2} & & \\
F_{2} & & \\
Cl_{2} & & \\
\end{array}
\]

Conversely, the eigenvector \( e_{2σ} \) corresponds to the direction along which the electrons at the BCP are subject to the least compressive forces. Therefore, \( e_{2σ} \) corresponds to the direction along which the BCP electrons will be least readily displaced when the BCP undergoes a torsion distortion. The bond-flexing \( F_{σ} \) associated with \( e_{2σ} \) is defined as:

\[
F_{σ} = [(e_{2σ} \cdot dr)_{\text{max}}]_{\text{CCW}} - [(e_{2σ} \cdot dr)_{\text{max}}]_{\text{CW}}
\] (4)
The bond-flexing $F_\sigma$ is calculated from the torsion $BCP$ bond flexing defined by equation (4); see Figures 1 and 2. Equation (4) provides a $U_\sigma$-space measure of the ‘flexing-strain’ or bond bending that a bond path is under in the cis- or trans-isomer configurations. This is consistent with greater ‘flexing-strain’ or bond bending that previously correlated with a greater presence of the cis-effect [18]. Higher values of $F_\sigma$ correspond to the dominance of the cis-isomer compared with the trans-isomer in $U_\sigma$ space, because bond bending reflects the symmetry of the cis-isomer rather than the trans-isomer, with respect to the positioning of the halogen substituents.

The bond-axiality $A_\sigma$ is part of the $U_\sigma$-space distortion set $\sum[T_\sigma,F_\sigma,A_\sigma]$, which provides a measure of the chiral asymmetry. It is defined as:

$$A_\sigma = [(e_{3\sigma} \cdot dr)_{\text{max}}]_{\text{CCW}} - [(e_{3\sigma} \cdot dr)_{\text{max}}]_{\text{CW}}$$

Equation (5) quantifies the direction of axial displacement of the bond critical point (BCP) in response to the bond torsion (CCW vs. CW), i.e., the sliding of the BCP along the bond path. We will, however, not use $A_\sigma$ as it does not comprise the bond cross-section, but provide it in the Supplementary Materials S5 and S6. Instead, we will use the so-called $U_\sigma$-space bond cross-section set $\sum[T_\sigma,F_\sigma]$ developed for cis- and trans-isomers.

The (+/-) sign of the bond-twist $T_\sigma$ and bond-flexing $F_\sigma$ determines the $S_\sigma$ ($T_\sigma > 0$, $F_\sigma > 0$) or $R_\sigma$ ($T_\sigma < 0$, $F_\sigma < 0$) character; see Tables 1 and 2.

The bond cross-section set $\sum[T_\sigma,F_\sigma]$ is related to the cross-section of a $BCP$ bond path that is quantified by the $\lambda_{1\sigma}$ and $\lambda_{2\sigma}$ eigenvalues associated with the $e_{1\sigma}$ and $e_{2\sigma}$ eigenvectors, respectively. Note, the $e_{1\sigma}$ and $e_{2\sigma}$ eigenvectors are the directions along which the $BCP$ electrons are displaced most readily and least readily, respectively, when the $BCP$ is subject to a torsional distortion. The trans-isomer is dominant in $U_\sigma$ space if the magnitude of the bond-twist $T_\sigma$ value is larger for the trans- than for the cis-isomer. Conversely, dominance of the cis-isomer is determined by the presence of a larger magnitude bond-flexing $F_\sigma$ value for the cis-isomer compared with the trans-isomer; see Tables 1 and 2.

2.2. Computational Details

The electronic wavefunction for molecular structures incorporating a chemically conventional double bond is usually well-represented by a single-reference wavefunction in the ‘eclipsed’ configurations 0° (cis) or 180° (trans). It is also well-known that as the dihedral angle across the double bond deviates from the ‘eclipsed’ configurations, the nature of the wavefunction changes, becoming fully multi-reference in nature at the twisted 90° ‘staggered’ configuration. The multi-reference character is determined for ethene using the frequently used T1 measure [36], where values of $T1 > 0.02$ indicate that a single-reference description is inadequate. For this reason, in all of this work, for both the $C_2X_2$ ($X = H, F, Cl$) and $N_2X_2$ ($X = H, F, Cl$) molecules, we use a multi-reference CAS-SCF(2,2) method [37,38], using Slater determinants for the active space, implemented in Gaussian G09.E01 [39] with symmetry disabled, an ‘ultrafine’ integration grid and convergence criteria of ‘VeryTight’ geometry convergence and an SCF convergence criterion of 10⁻¹². The cc-pVTZ triple-zeta basis set was used during geometry optimization and the dihedral coordinate scan constrained geometry optimization process. The magnitude of the dihedral angle scan steps was 1°. Additionally, the second atom used in each sequence defining the dihedral scan angle, C1 and N1, respectively, for the ethene and diazene derivatives, was constrained to be fixed at the origin of the Cartesian spatial coordinates. All initial ‘eclipsed’ (cis- and trans-) optimized molecular geometries were generated (and checked to be energy minima with no imaginary vibrational frequencies) with these settings; see Supplementary Materials S2 for the optimized structures and tabulated experimental data. The final single-point wavefunctions and densities for each structure produced during the dihedral scans were calculated, as recommended for accurate NG-QTAIM properties [40], using a quadruple-zeta basis set (cc-pVQZ).

The direction of torsion is determined to be CCW (0.0° ≤ $\theta$ ≤ +90.0°) or CW (−90.0° ≤ $\theta$ ≤ 0.0°) from an increase or a decrease in the dihedral angle, respectively. An exception is made for
N₂Cl₂ where the respective angular limits used were −80° and +80°. These latter limits are chosen due to the well-known destabilizing interactions between the nitrogen lone pairs and the relatively weak N-Cl bonds [41,42], which cause dissociation of the molecule into N₂ and Cl₂ when a larger twist is applied: we observed and confirmed this dissociation for dihedral twists > 80°.

The stress tensor trajectories T_σ(s) for all four of the possible ordered sets of four atoms that define the dihedral angle for each of the cis-isomers (X3-C1-C2-X6, X3-C1-C2-H5, H4-C1-C2-H5, H4-C1-C2-X6) and trans-isomers (X4-C1-C2-X6, X4-C1-C2-H5, H3-C1-C2-H5, H3-C1-C2-X6) are calculated; see the left panel of Scheme 1 for the dihedral atom numbering. There is a single dihedral X3-N1-N2-X4 for each of the cis- and trans-isomers of the diazenes N₂X₂ (X = H, F, Cl); see the right panel of Scheme 1.

QTAIM and stress tensor analysis were then performed on each single-point wavefunction obtained in the previous step with the AIMAll [33] and QuantVec [43] suite. In addition, all molecular graphs were confirmed to be free of non-nuclear attractor critical points.

3. Results and Discussions

The scalar distance measures geometric bond length (GBL) and bond path length (BPL) used in this investigation on ethene, doubly substituted ethene and diazene are insufficient to quantify the presence of the cis-effect and are provided in the Supplementary Materials S3. The variation in the (scalar) relative energy ΔE for ethene, doubly substituted ethene and diazene molecules do not provide any insights either into the cis-effect for these molecules and are provided in the Supplementary Materials S4. The intermediate and the complete C1-C2 BCP U_σ-space distortion sets are provided in the Supplementary Materials S5 and S6, respectively.

The sum of the bond-cross-section sets ∑T_σ,F_σ of the C1-C2 BCP T_σ(s) was calculated for all four possible isomers of the formally achiral molecules ethene and doubly substituted ethane, C₂X₂ (X = H, F, Cl). The results for the molecular graph of pure ethene are provided as a control to enable a better understanding of the effect of the halogen atom substitutions; see Table 1 and Scheme 1. The corresponding results for the formally achiral diazenes N₂X₂ (X = H, F, Cl) comprising a single isomer N1-N2 BCP T_σ(s) are presented in Table 2. The magnitude of the values of the bond cross-section set ∑T_σ,F_σ increases with atomic weight, as is demonstrated for F₂ and Cl₂ substitution of ethene; see Table 1. This relationship between the magnitude of the ∑T_σ,F_σ values and halogen substituent also occurred in a recent investigation of singly and doubly halogen-substituted ethane [44]. This dependency of ∑T_σ,F_σ on the atomic weight of the substituent, however, does not occur for the diazenes.

The magnitude of the bond-twist T_σ is significantly smaller for the cis-compared with the trans-isomer for C₂X₂ (X = F, Cl) and slightly smaller for N₂X₂ (X = Cl). The magnitude of the bond-flexing F_σ is significantly larger for the cis-compared with the trans-isomer for C₂X₂ (X = F, Cl) and N₂X₂ (X = F, Cl).

These results for the bond cross-section set ∑T_σ,F_σ are consistent with the presence of the cis-effect and therefore indicate the occurrence of the cis-effect in U_σ space for C₂X₂ (X = H, Cl) and N₂X₂ (X = H, Cl). The very large component of the bond-twist T_σ for N₂X₂ (X = H) indicates a complete lack of the cis-effect and a dominance of the trans-isomer in U_σ space for this molecule.

All of the investigated molecular graphs comprised a significant degree of chiral character as indicated by the magnitudes of the bond-twist T_σ and bond-flexing F_σ, particularly for C₂X₂ (X = F, Cl).

4. Conclusions

In this investigation, NG-QTAIM was used to determine the presence or absence of the cis-effect for the C₂X₂ (X = H, F, Cl) and N₂X₂ (X = H, F, Cl) molecules. Qualitative agreement with experimental data for differences in the energies of the cis- and trans-isomers was found.
The molecules of this investigation are formally achiral according to the Cahn–Ingold–Prelog (CIP) priority rules [45], but all comprise at least a degree of chiral character in \( U_\sigma \) space, on the basis of the magnitude of the \( T_\sigma \) values, with \( \text{C}_2\text{H}_2(X = \text{Cl}) \) displaying a very significant degree of chirality. This finding reflects the conventional understanding that steric effects are among the reasons for the differences between the relative energetic stabilities of cis- and trans-isomers, consistent with our previous association of chiral character in \( U_\sigma \) space for the steric effects for ethane [20].

We found that both \( \text{C}_2\text{H}_2(X = \text{F}, \text{Cl}) \) and \( \text{N}_2\text{H}_2(X = \text{F}, \text{Cl}) \) display the cis-effect. This includes the prediction of a cis-effect in \( \text{N}_2\text{X}_2(X = \text{Cl}) \), for which no experimental data on the cis-isomer and trans-isomer energy difference are available. The cis-effect is determined on the basis of the much larger values of the bond-flexing \( F_\sigma \) for the cis- compared with the trans-isomer.

We provided a physical explanation as to why the cis-effect is the exception rather than the rule, by defining a dominant bond-flexing \( F_\sigma \) component of the bond cross-section set \([T_\sigma,F_\sigma]\) as characterizing the cis-effect. This is on the basis that it is more difficult to bend \( (F_\sigma) \) than to twist \( (T_\sigma) \) the C1-C2 BCP bond path and N1-N2 BCP bond path. This difference in the difficulty of performing bond-bending \( (F_\sigma) \) and bond-twisting \( (T_\sigma) \) distortions is explained by their construction, using the least preferred \( e_2\sigma \) and most preferred \( e_1\sigma \) eigenvectors, respectively, that determine the relative ease of motion of the electronic charge density \( \rho(r_b) \).

Suggestions for future work include the exploration of the newly discovered NG-QTAIM bond cross-section set \([T_\sigma,F_\sigma]\) for cis- and trans-isomers, which could be undertaken by manipulating the cis- and trans-isomer character in \( U_\sigma \) space with laser irradiation. We make this suggestion since NG-QTAIM chirality has already been found to be reversed by the application of an electric field [46]. Reversing the cis- and trans-isomer character in \( U_\sigma \) space is possible with laser irradiation that is fast enough to avoid disrupting atomic positions. Such a reversal in \( U_\sigma \) space could result in the cis- and trans-geometric isomers comprising trans- and cis-isomer assignments in \( U_\sigma \) space, respectively.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/molecules27186099/s1, S1. NG-QTAIM and stress tensor theoretical background and procedure to generate the stress tensor trajectories \( T_\sigma(\phi) \). S2. Experimental data, geometry optimized structures for ethene, doubly substituted ethene and diazene. S3. Distance measures for ethene, doubly substituted ethene and diazene. S4. Scalar measures (relative energy \( \Delta E \)) for ethene, doubly substituted ethene and diazene. S5 The maximum stress tensor projections \( T_\sigma(\phi)_{\text{max}} \) for ethene, doubly substituted ethene and diazene. S6. Tables of the complete C1-C2 BCP \( U_\sigma \)-space distortion sets for ethene and doubly substituted ethene and diazene. References [47–59] are cited in the Supplementary Materials.

**Author Contributions:** Conceptualization, S.R.K. and S.J.; Data curation, Y.P., W.Y., X.F. and T.X.; Investigation, Y.P., W.Y., X.F., T.X., H.F., T.v.M., S.R.K. and S.J.; Methodology, S.J.; Supervision, S.R.K. and S.J.; Writing—original draft, S.J.; Writing—review and editing, H.F., T.v.M. and S.R.K. All authors have read and agreed to the published version of the manuscript.

**Funding:** The Hunan Natural Science Foundation of China project approval number: 2022JJ30029. The One Hundred Talents Foundation of Hunan Province is also gratefully acknowledged for the support of S.J. and S.R.K. H.F. and T.v.M. gratefully acknowledge computational support via the EaStCHEM Research Computing Facility.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Not applicable.

**Acknowledgments:** The Hunan Natural Science Foundation of China is gratefully acknowledged, project approval number: 2022JJ30029. The One Hundred Talents Foundation of Hunan Province is also gratefully acknowledged for the support of S.J. and S.R.K. H.F. and T.v.M. gratefully acknowledge computational support via the EaStCHEM Research Computing Facility.
Conflicts of Interest: The authors declare no conflict of interest.

Sample Availability: Samples of the compounds are available from the authors.

References

1. Garcia-Fernandez, P.; Liu, Y.; Bersuker, I.B.; Boggs, J.E. Pseudo Jahn–Teller Origin of Cis–Trans and Other Conformational Changes. The Role of Double Bonds. *Phys. Chem. Chem. Phys.* 2011, 13, 3502–3513. [CrossRef] [PubMed]

2. Feller, D.; Peterson, K.A.; Dixon, D.A. Ab Initio Coupled Cluster Determination of the Heats of Formation of C2H2F2, C2F2, and C2F4. *J. Phys. Chem. A* 2011, 115, 1440–1451. [CrossRef] [PubMed]

3. Yamamoto, T.; Kaneno, D.; Tomoda, S. The Origin of Cis Effect in 1,2-Dihaloethenes: The Quantitative Comparison of Electron Delocalizations and Steric Exchange Repulsions. *Bull. Chem. Soc. Jpn.* 2008, 81, 1415–1422. [CrossRef]

4. Zhao, D.B.; Rong, C.Y.; Jenkins, S.; Kirk, S.R.; Yin, D.L.; Liu, S.B. Origin of the Cis-Effect: A Density Functional Theory Study of Doubly Substituted Ethylenes. *Acta Phys. Chim. Sin.* 2013, 29, 43–54. [CrossRef]

5. Banerjee, D.; Ghosh, A.; Chattopadhyay, S.; Ghosh, P.; Chaudhuri, R.K. Revisiting the ‘Cis–Effect’ in 1,2-Difluoro Derivatives of Ethylene and Diazone Using Ab Initio Multireference Methods. *Mol. Phys.* 2014, 112, 3206–3224. [CrossRef]

6. Tavanaei, L.; Nori-Shargh, D. New Insights into the Origin of the Cis-Configuration Preferences in 1,2-Dihaloethenes: The Importance of the Bonding Orbital Deviations. *Aust. J. Chem.* 2018, 71, 1–13. [CrossRef]

7. Tavares, L.; Nori-Shargh, D. New Insights into the Origin of the Cis-Configuration Preferences in 1,2-Dihaloethenes: The Importance of the Bonding Orbital Deviations. *Aust. J. Chem.* 2018, 71, 1–13. [CrossRef]

8. Craig, N.C.; Piper, L.G.; Wheeler, V.L. Thermodynamics of Cis-Trans Isomerizations. II. 1-Chloro-2-Fluoroethylenes, 1,2-Difluorocyclopropanes, and Related Molecules. *J. Phys. Chem.* 1971, 75, 1453–1460. [CrossRef]

9. Craig, N.C.; Entemann, E.A. Thermodynamics of Cis-Trans Isomerizations. The 1,2-Difluoroethylenes. *J. Am. Chem. Soc.* 1961, 83, 3047–3050. [CrossRef]

10. Craig, N.C.; Overend, J. Vibrational Assignments and Potential Constants for Cis- and Trans-1,2-Difluoroethylenes and Their Deuterated Modifications. *J. Chem. Phys.* 1969, 51, 1127–1142. [CrossRef]

11. Craig, N.C.; Chen, A.; Suh, K.H.; Klee, S.; Mellau, G.C.; Winnewisser, B.P.; Winnewisser, M. Complete Structure of the Anti Rotamer of 1,2-Difluoroethane from High-Resolution Infrared Spectroscopy. *J. Phys. Chem. A* 1997, 101, 9302–9308. [CrossRef]

12. Craig, N.C.; Li, Z.; Xu, T.; Früchtl, H.; von Mourik, T.; Kirk, S.R.; Rong, C.Y.; Jenkins, S.; Yin, D.L.; Liu, S.B. Origin of the Cis-Effect: A Density Functional Theory Study of Doubly Substituted Ethylenes. *Acta Phys. Chim. Sin.* 2013, 29, 43–54. [CrossRef]

13. Garcia-Fernandez, P.; Liu, Y.; Bersuker, I.B.; Boggs, J.E. Pseudo Jahn–Teller Origin of Cis–Trans and Other Conformational Changes. The Role of Double Bonds. *Phys. Chem. Chem. Phys.* 2011, 13, 3502–3513. [CrossRef] [PubMed]

14. Gardner, D.V.; McGreer, D.E. Influence of Steric and Polar Effects in Determining the Equilibrium Position for Cis-Trans-Olefins Pairs. *Can. J. Chem.* 1970, 48, 2104. [CrossRef]

15. Gardner, D.V.; McGreer, D.E. Influence of Steric and Polar Effects in Determining the Equilibrium Position for Cis-Trans-Olefins Pairs. *Can. J. Chem.* 1970, 48, 2104. [CrossRef]

16. Waldron, J.T.; Snyder, W.H. Thermodynamics of Cis-Trans Isomerizations. Relative Stabilities of the 1,2-Dimethoxyethylenes. *J. Am. Chem. Soc.* 1973, 95, 5491–5495. [CrossRef]

17. Tokuhashi, K.; Uchimaru, T.; Takizawa, K.; Kondo, S. Rate Constants for the Reactions of OH Radicals with the (E)/(Z) Isomers of CFC=CFCI and (E)-CHF=CHF. *J. Phys. Chem.* 1970, 74, 1712–1727. [CrossRef]

18. Jenkins, S.; Kirk, S.R.; Rong, C.; Yin, D. The Cis-Effect Using the Topology of the Electronic Charge Density. *Mol. Phys.* 2012, 111, 1–13. [CrossRef]

19. Gardiner, D.V.; McGreer, D.E. Influence of Steric and Polar Effects in Determining the Equilibrium Position for Cis-Trans-Olefins Pairs. *Can. J. Chem.* 1970, 48, 2104. [CrossRef]

20. Banerjee, D.; Ghosh, A.; Chattopadhyay, S.; Ghosh, P.; Chaudhuri, R.K. Revisiting the ‘Cis–Effect’ in 1,2-Difluoro Derivatives of Ethylene and Diazone Using Ab Initio Multireference Methods. *Mol. Phys.* 2014, 112, 3206–3224. [CrossRef]

21. Garcia-Fernandez, P.; Liu, Y.; Bersuker, I.B.; Boggs, J.E. Pseudo Jahn–Teller Origin of Cis–Trans and Other Conformational Changes. The Role of Double Bonds. *Phys. Chem. Chem. Phys.* 2011, 13, 3502–3513. [CrossRef] [PubMed]

22. Feller, D.; Peterson, K.A.; Dixon, D.A. Ab Initio Coupled Cluster Determination of the Heats of Formation of C2H2F2, C2F2, and C2F4. *J. Phys. Chem. A* 2011, 115, 1440–1451. [CrossRef] [PubMed]

23. Yamamoto, T.; Kaneno, D.; Tomoda, S. The Origin of Cis Effect in 1,2-Dihaloethenes: The Quantitative Comparison of Electron Delocalizations and Steric Exchange Repulsions. *Bull. Chem. Soc. Jpn.* 2008, 81, 1415–1422. [CrossRef]

24. Zhao, D.B.; Rong, C.Y.; Jenkins, S.; Kirk, S.R.; Yin, D.L.; Liu, S.B. Origin of the Cis-Effect: A Density Functional Theory Study of Doubly Substituted Ethylenes. *Acta Phys. Chim. Sin.* 2013, 29, 43–54. [CrossRef]

25. Tavares, L.; Nori-Shargh, D. New Insights into the Origin of the Cis-Configuration Preferences in 1,2-Dihaloethenes: The Importance of the Bonding Orbital Deviations. *Aust. J. Chem.* 2018, 71, 1–13. [CrossRef]

26. Garcia-Fernandez, P.; Liu, Y.; Bersuker, I.B.; Boggs, J.E. Pseudo Jahn–Teller Origin of Cis–Trans and Other Conformational Changes. The Role of Double Bonds. *Phys. Chem. Chem. Phys.* 2011, 13, 3502–3513. [CrossRef] [PubMed]
56. Xu, T.; Momen, R.; Azizi, A.; van Mourik, T.; Früchtl, H.; Kirk, S.R.; Jenkins, S. The Destabilization of Hydrogen Bonds in an External E-Field for Improved Switch Performance. *J. Comput. Chem.* **2019**, *40*, 1881–1891. [CrossRef] [PubMed]

57. Tian, T.; Xu, T.; van Mourik, T.; Früchtl, H.; Kirk, S.R.; Jenkins, S. Next Generation QTAIM for the Design of Quinone-Based Switches. *Chem. Phys. Lett.* **2019**, *722*, 110–118. [CrossRef] [PubMed]

58. Yang, W.; Zurbenko, I. Kolmogorov–Zurbenko Filters. *WIREs Comp. Stat.* **2010**, *2*, 340–351. [CrossRef]

59. Tian, T.; Xu, T.; Kirk, S.R.; Rongde, I.T.; Tan, Y.B.; Manzhos, S.; Shigeta, Y.; Jenkins, S. Intramolecular Mode Coupling of the Isotopomers of Water: A Non-Scalar Charge Density-Derived Perspective. *Phys. Chem. Chem. Phys.* **2020**, *22*, 2509–2520. [CrossRef] [PubMed]