Steric Interactions between \(sp\) and \(sp^3\) Carbons in Acyclic Alkynes and Nitriles

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A B S T R A C T

Each atom within a molecule occupies a definite volume in space. As a result, an unfavorable interaction would be expected when atoms are placed too close together. This paper explores various conformations of acyclic alkynes and aliphatic nitriles in order to obtain the most stable geometries, utilizing the supposition that molecules prefer to minimize steric strain. The two conformations of interest in this study are synclinal and antiperiplanar interactions, which are theoretically the most stable geometries. However, \textit{ab initio} calculations utilizing the 3-21G basis set for geometry optimizations show that the most stable conformations do not necessarily prefer maximizing distances between carbon atoms. The molecules analyzed consist of twenty 1-alkynes, one 2-alkyne, and sixteen nitriles that range from 5 to 9 carbon atoms. For each molecule, the three most stable conformations were found by \textit{ab initio} geometry optimizations. On the one hand, even after taking into account the zero-point energy corrections for 1-alkynes in the gas phase, the calculations predict that \(sp\)/(\(sp^3\)) synclinal interactions are stabilizing relative to fully extended (antiperiplanar) conformations. The effects of \(sp\)/(\(sp^3\)) synclinal and gauche interactions do not appear to be additive for 1-alkynes. On the other hand \(sp\)-\(sp^3\) synclinal interactions in nitriles do not have a large effect (neither stabilizing nor destabilizing). The effects of \(sp\)/(\(sp^3\)) synclinal and gauche interactions appear to be additive for nitriles.

F A C U L T Y  M E N T O R

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Tom Morton has been on UCR’s chemistry faculty for 30 years. Since 2006 he has been teaching, on top of a large undergraduate organic chemistry lecture, Honors discussion sections for organic chemistry (Chem 122H, 123H, and 124H). In these discussion sections each student performs an original computational investigation. The present work embraces an analysis of results obtained by the approximately 45 students enrolled in Chem 122H in fall, 2010.

Pictured above from bottom left to right: Daniya Ashhad, Emelline Chen, Leila Magistrado, Adam Silvers
Top from left to right: Mundy Reimer, Jonathan Getscher, Christopher Margono
INTRODUCTION

Each atom within a molecule occupies a definite volume in space. As a result, one would expect unfavorable interaction when atoms within a molecule become too close to each other. Interactions of this nature fall into two categories, torsional strain (between adjacent \(sp^3\) centers) and steric strain (between non adjacent strain). Steric strain is defined as the “repulsive interaction that occurs when atoms are forced closer together than their atomic radii allow. It is the result of trying to force two atoms to occupy the same space” [1]. This paper explores various conformations of acyclic molecules in order to obtain the most stable geometries utilizing the supposition that molecules prefer to minimize steric strain. However, using \textit{ab initio} calculations of the 3-21G basis set for geometry optimizations, we found that the most stable molecules do not necessarily prefer maximizing distances between carbon atoms. The goal of this work is to explore \(sp-sp^3\) steric interactions [which will be denoted as \(sp)(sp^3\)] in acyclic alkynes and aliphatic nitriles.

The two conformations of interest are synclinal and antiperiplanar as shown in Figure 1. Although we are interested in acyclic interactions, observing a substituent on a cyclohexane ring can give general insight into how a substituent behaves. To investigate the conformations of interest, we looked at their A-values, which quantify the steric strain of a substituent on a cyclohexane ring. The A-values for a cyano group (-C≡N) and an ethynyl group (-C≡CH) are both positive, indicating that these substituents prefer equatorial rather than axial positions on a cyclohexane chair [2]. However it is important to note that the preferred conformation of pentyne leads to the observation that \(sp)(sp^3\) synclinal interactions appear to have a stabilizing effect in acyclic hydrocarbons [3].

3-21G calculations of axial versus equatorial methylecyclohexane agree with the A-values obtained through Nuclear Magnetic Resonance (NMR) denoted in scientific literature: a methyl group prefers to be in the equatorial position. However, contrary to NMR, the results for an ethynyl or cyano group indicate that these groups prefer axial rather than equatorial positions. In essence, while 3-21G calculations show that methylecyclohexane agrees quantitatively with published A-values [2], cyano- and ethynyl cyclohexane disagree with what the solution phase NMR spectra show.

There are a number of reasons for such discrepancies. First, the 3-21G calculations examine an isolated molecule as opposed to molecules in solution. Differences in A-values for \(-CCH\) and \(-CN\), which are determined by using \(^{13}\text{C}\) NMR, may be attributed to the presence of a solvent. A second possible explanation may be that the calculated electronic energies do not take into account entropy, while the A-values do. A third possible explanation may be that the electronic energies calculated do not take zero-point energy (ZPE) into account. ZPE refers to lowest energy of the ground state as opposed to fluctuations of electrons that result in excited states.

The following survey of 3-21G calculations seeks to further explore the interactions of \(sp\) hybridized carbons with \(sp^3\) hybridized carbons in a series of acyclic monoalkynes and acyclic nitriles. We used the 3-21G calculations due to its optimization of steric geometry for the molecules given. This is based on the assumption that steric interactions in a monosubstituted cyclohexane are equivalent to steric interactions in acyclic molecules. However, this assumption may in actuality be incorrect. That inference is one of the possible conclusions drawn from the work described below.

METHODS

The molecules analyzed include all constitutional isomers of all the 1-alkynes and nitriles that range from five to nine carbons. A subset was selected to consist of molecules that
STERIC INTERACTIONS BETWEEN SP AND SP3 CARBONS IN ACYCLIC ALKynes AND NITRILES

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did not apparently exhibit unusual intramolecular steric interactions. We chose twenty1-alkynes, one 2-alkyne, and sixteen nitriles to survey, which, to our knowledge, has not been done before. For each molecule, the three most stable conformations were found by geometry optimizations that manipulate bond lengths, bond angles, and torsional angles of the molecule using 3-21G method to calculate the electronic energies [4] by means of the Spartan software [5]. The three most stable conformations of a molecule (those having the most negative electronic energies) were then examined to evaluate their stabilities relative to the most stable conformation. The relative energies of the higher energy conformers were determined by taking the electronic energy differences between that conformer and the most stable one.

In order to compare the effects of different types of interactions, each conformation was examined to see what interactions were present. The differences between the pairs of conformers were categorized in terms of three interactions: gauche [interactions between hydrogens on sp3 centers, sp3(sp3), sp(sp3) synclinal, and 1,5-sp(sp3).

RESULTS

The effects of the aforementioned interactions either stabilize or destabilize the conformer. A gauche interaction describes the steric interaction of hydrogenson sp3 carbons that have a dihedral angle of approximately ±60°. Because of the proximity of the hydrogen atoms steric strain results [1], i.e. destabilizing the conformer. There is a gauche interaction between the hydrogens on C2 and C5 in Figure 2a below. An sp) (sp3 synclinal interaction occurs between an sp carbon and an sp3 carbon with a dihedral angle of approximately ±60°. This interaction is present between C1 and C4 in Figure 2A below. Contrary to our initial assumption, this interaction is found to be stabilizing [3]. Holme et. al propose that the stabilizing effect may be due to the “attractive electrostatic interaction between the methyl and acetylenic [functional groups].” [3] The last interaction we examined in alkynes and nitriles is 1,5-sp(sp3. This interaction is very similar in principle to a gauche. However, it is not called as such because a gauche interaction is between sp3 carbons. In a 1,5- sp(sp3 interaction, as shown in Figure 2b between hydrogens on C1 and a hydrogen on C5, the sp and sp3 are oriented too close to each other in space, therefore destabilizing the conformer. In the data tables, which are found on the University Honors website (http://honors.ucr.edu/classes/URJ_Tables_Revised.pdf) [6], these three interactions are enumerated relative to the most stable conformation.

Fig. 2: (a) sp(sp3 synclinal interaction between C1 and C4 (a gauche interaction); (b) 1,5- sp(sp3 interaction between C1 and C5 (no gauche interaction). The same holds true for alkynes, but replacing nitrogen (N) with an sp-carbon bonded to a hydrogen (CH)

These differences were then used to find the average effect of each interaction. The results are summarized in Figure 1. The gauche and sp(sp3 synclinal interactions were separately averaged for 1-alkynes and nitriles to determine and compare the effects of both interactions on each type of molecule. Thirteen 1-alkynes and six 1-alkynes differ from the most stable conformation by a single gauche (denoted as a 1/0/0) and a single sp(sp3 synclinal (denoted as 0/-1/0), respectively. The analysis of the data for these conformers show that the gauche interaction is destabilizing by 0.0012 a.u, whereas the sp(sp3 synclinal is stabilizing by 0.00052 a.u . Twelve nitriles and six nitriles from the table found on the University Honors Website [6] differ from the most stable conformation by a single gauche and single sp(sp3 synclinal, respectively. The data of the nitrile analysis qualitatively agrees with the alkyn data in that a gauche interaction is destabilizing (by 0.0012 a.u.) whereas the sp(sp3 synclinal interaction is stabilizing (by 0.000044 a.u.).

The question is then raised whether a conformer which has gained a gauche and lost a sp(sp3 synclinal interaction (denoted as 1/-1/0) would have an additive effect of these two interactions. For the nitriles, we predicted a quantitative electronic energy value by simply adding the absolute value of the average of the energy changes
for a gauche and an \( sp(sp^3 \) synclinal. We concluded that 1/-1/0 conformer should be 0.0013 a.u. greater in energy than the lowest conformation. The actual energy for a 1/-1/0 conformer determined by averaging all of their energies is predicted to be +0.0015 a.u. Therefore, the data suggests that a gauche interaction and \( sp(sp^3 \) synclinal interaction are, in fact, additive for nitriles. The same calculations were done for the alkynes. The predicted sum for 1-alkynes is 0.0017 a.u. (SD: 0.00040 a.u.), whereas the calculated value (the average of the 1/-1/0 conformation data) is 0.0013 a.u. (SD: 0.00032 a.u.). We want to compare the calculated values with the predicted sum. When looking at the distribution of the calculated 1-alkyne data of the 1/-1/0 conformations, it turns out that there are many points that lie outside of one standard deviation of the predicted sum. In this distribution of relative electronic energy difference values, there are ten 1/-1/0 1-alkyne conformations that were analyzed to determine the calculated average, which only one is higher than the predicted sum. There are two calculated values that lie within one standard deviation below the predicted sum. On a statistical basis, our electronic energy calculations do not suggest that the effects of the two interactions are additive.

<table>
<thead>
<tr>
<th></th>
<th>Alkynes (kJ/mol)</th>
<th>Nitriles (kJ/mol)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>gauche</td>
<td>+3.15 (SD: 0.45)</td>
<td>+0.001199 (SD: 0.000173)</td>
</tr>
<tr>
<td></td>
<td>+3.00</td>
<td>+0.001141 (SD: 0.000133)</td>
</tr>
<tr>
<td>sp(sp^3</td>
<td>-1.37 (SD: 0.94)</td>
<td>-0.000522 (SD: 0.000359)</td>
</tr>
<tr>
<td></td>
<td>-0.44</td>
<td>-0.000166 (SD: 0.000044)</td>
</tr>
<tr>
<td>Predicted Sum</td>
<td>+4.52 (SD: 1.04)</td>
<td>+0.001720 (SD: 0.000399)</td>
</tr>
<tr>
<td></td>
<td>+3.43</td>
<td>+0.001307 (SD: 0.000140)</td>
</tr>
<tr>
<td>Actual Sum</td>
<td>+3.33 (SD: 0.85)</td>
<td>+0.001270 (SD: 0.000323)</td>
</tr>
<tr>
<td></td>
<td>+3.95</td>
<td>+0.001504 (SD: 0.000192)</td>
</tr>
</tbody>
</table>

Table 1. Average effects of each interaction and their additives

**DISCUSSION**

The relative \( \Delta E^d \) for methyl-, cyano-, and ethynylcyclohexane were determined by the 3-21G method in order to compare their A-values. The A-value obtained for methylcyclohexane (8.02 kJ/mol) agrees with the experimental A-value (7.28 kJ/mol) [7]. The calculated A-value we obtained for methylcyclohexane is also approximately twice the energy of two gauches in butane. This predicts that cyclohexane is a strain free ring and an axial methyl group is less preferred than an equatorial methyl group.

The most recent experimental A-values, (based on \(^{13}C\) NMR in CFCl₃ solution) for cyanocyclohexane (0.90±0.08 kJ/mol) [8] and ethynylcyclohexane (2.16±0.05 kJ/mol) [8] imply that the equatorial cyclohexane chair conformation is preferred over the axial. Neither does this agree with what the calculated relative \( \Delta E^d \) (kJ/mol) predicts [axial is preferred over equatorial], nor does it agree with what our data suggests [an \( sp(sp^3 \) synclinal interaction is stabilizing]. We looked at factors that could account for the incongruity between \( sp(sp^3 \) steric interactions in acyclic compounds and those in cyclic compounds. We concluded that there are three factors that could possibly cause this discrepancy.

The first one is that entropy was not taken into account for the electronic energies, whereas the experimental A-values incorporate entropy. The second factor is that the electronic energies determined using the 3-21G method look at an isolated, gaseous molecule as opposed to a molecule in solution. The third possible explanation may be that the electronic energies calculated do not take ZPE into account. Entropy of a molecule plays a role in determining stability. However, there is no entropy change between axial and equatorial for cyanocyclohexane [7]. Therefore, the entropy cannot be a reason for the discrepancy, so we must further analyze the other explanations.

Selected compounds in the table on the University Honors Website [6] were used in order to analyze the effects of ZPE and to see whether they shift the data one way or another. Two alkyn example chosen are 1-pentyne and 1-nonyne. The ZPE corrections are found to be non-negligible. The electronic energy difference found by the 3-21G method of 1-pentyne with a \( sp(sp^3 \) synclinal interaction is 1.0 kJ/mol (0.000378 a.u.). By taking into account the 0.61 kJ/mol (0.000231 a.u.) ZPE destabilization of the conformation with a \( sp(sp^3 \) synclinal interaction relative to the fully extended conformation, the corrected value for the enthalpy difference for the two conformers of 1-pentyne is 0.39 kJ/mol (0.000147 a.u.) in favor of the \( sp(sp^3 \) synclinal conformation. This value agrees with the experimental value of 0.50 ± 0.36 kJ/mol for gaseous 1-pentyne [3].
The energy for 1-nonyne is also corrected by taking into account the ZPE. 1-Nonyne with an \( sp / sp^3 \) synclinal interaction is preferred over the fully extended conformation by an electronic energy difference of 0.63 kJ/mol. However, the ZPE correction, which turns out to be the same as for 1-pentyne (0.61 kJ/mol), predicts that 1-nonyne prefers synclinal by only 0.02 kJ/mol. 1-Nonyne has the smallest electronic energy difference between the fully extended and the \( sp / sp^3 \) synclinal. 1-P entyne and 1-nonyne both show the same ZPE correction of 0.61 kJ/mol, this correction appears to be substantially less than the average electronic energy of \( sp / sp^3 \) synclinal stabilization, 1.4 kJ/mol. However, even with ZPE corrections, the 3-21G method predicts that \( sp / sp^3 \) synclinal interactions stabilize acyclic 1-alkynes in the gas phase.

Two nitriles were also selected to observe the effects of ZPE corrections. These examples include 1-butononitrite and 1-nonanonitrile. The consequence of ZPE corrections for the nitriles does not have the same results as they do for the 1-alkynes. When analyzing electronic energies, there was a distinct difference between the relative energies of a gauche and \( sp / sp^3 \) synclinal conformation. However, the ZPE correction practically eliminated the difference of electronic energy between the fully extended and synclinal. The differences between the electronic energy and ZPE for the synclinal and fully extended conformations are equal and opposite, therefore making both conformations have the same heats of formation, \( \Delta f H^0 \). Unlike for the alkynes, the nitriles are predicted to have the same stability for fully extended and \( sp / sp^3 \) synclinal conformation even after corrections made by ZPE’s.

ZPE energy corrections for cyano-, methyl-, and ethynlycyclohexane were also calculated using the 3-21G method. (They are summarized in Table 2.) The \( \Delta \text{ZPE} \) between axial and equatorial cyano-cyclohexane is 0.41 kJ/mol. Using the ZPE to correct the relative \( \Delta E_{el} \), cyano-cyclohexane still seems to prefer the axial conformation relative to the equatorial conformation. After taking into account the \( \Delta \text{ZPE} \) for methlycyclohexane, we calculated that even though the ZPE correction decreases the preference of equatorial conformation by 0.89 kJ/mol, it still predicts that methlycyclohexane prefers the equatorial by 7.13 kJ/mol. The \( \Delta \text{ZPE} \) between axial and equatorial ethynlycyclohexane is 0.87 kJ/mol. Taking this correction into consideration, it seems to appear that ethynlycyclohexane now prefers to be in equatorial conformation by 0.1 kJ/mol. This qualitatively agrees with the experimental A- value (2.16 ± 0.05 kJ/mol) [9] since both predict that the equatorial conformation is preferred. However, it is now in conflict with what we predicted for acyclic compounds (i.e., an \( sp / sp^3 \) synclinal is stabilizing). Despite qualitative agreement, the experimental A-value reported is much larger. It is determined by \(^{13}\text{C} \) NMR in CFCl\(_3\) solvent. This factor may play a role in the reason for the large difference between what we calculated (0.10 kJ/mol) and what is reported experimentally. In order to determine the effects of solvent, we calculated the dipole moments of the cyclohexane compounds.

A molecule that contains bonds in which a distance separates opposite charges possesses an electrical dipole moment. The magnitude of the charge and distance of separation between these charged centers is called the dipole moment, measured in units of debye (D). Dipole moments of the substituted cyclohexane compounds in axial and equatorial conformations were determined using the 3-21G method. (They are summarized in Table 2.) Methylcyclohexane has a dipole moment of 0.052 D in the equatorial conformation versus a dipole moment of 0.036 D in the axial conformation. The dipole moment for cyanocyclohexane is determined to be 4.33 D for the equatorial conformer as opposed to 3.98 D for the axial conformer, and for ethynlycyclohexane the dipole moment is suggested to be 0.83 D for the equatorial conformer as opposed to 0.60 D for the axial conformer. All three conformations have a higher dipole moment in the equatorial conformation. Since the NMR experiments had to be performed in solvent as opposed to in a gas, we surmise that the solvent may shift the equilibrium favor of the equatorial conformation due to the higher dipole moment of monosubstituted cyclohexanes.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Axial ( \Delta E_{el} ) (a.u.)</th>
<th>Equatorial ( \Delta E_{el} ) (a.u.)</th>
<th>Eq. ( \Delta E_{el} ) Eq. ( \Delta E_{el} )</th>
<th>Axial ( \Delta \text{ZPE} ) (kJ/mol)</th>
<th>Eq. ( \Delta \text{ZPE} ) (kJ/mol)</th>
<th>Dipole Moment (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethynlycyclohexane</td>
<td>-0.8170009</td>
<td>-0.808170015</td>
<td>-2.94 x 10^-4</td>
<td>-0.77</td>
<td>0.886</td>
<td>0.602</td>
</tr>
<tr>
<td>Cyanocyclohexane</td>
<td>-1.02437553</td>
<td>-1.02437591</td>
<td>-2.02 x 10^-4</td>
<td>-0.53</td>
<td>0.412</td>
<td>3.976</td>
</tr>
<tr>
<td>Methylcyclohexane</td>
<td>-2.71735060</td>
<td>-2.71735015</td>
<td>3.06 x 10^-3</td>
<td>0.085</td>
<td>-0.085</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Table 2. Monosubstituted cyclohexane conformational energies and dipole moments
CONCLUSIONS

Even after taking into account the ZPE corrections for 1-alkynes in the gas phase, the calculations predict that \( sp \) (\( sp^3 \) synclinal interactions are stabilizing relative to fully extended conformations. Quantitatively the prediction for 1-pentyne (0.39 kJ/mol) in the gas phase agrees with experimental results (0.50 ± 0.36 kJ/mol). [3] The effects of \( sp \)(\( sp^3 \) synclinal and gauche interactions do not appear to be additive for 1-alkynes. ZPE corrections for nitriles in the gas phase give calculated results that \( sp \) (\( sp^3 \) synclinal conformers are no more stable than the fully extended conformations. Hence, they have virtually the same \( \Delta H^\circ \). The synclinal conformation is slightly preferred over fully extended for nitriles by an electronic energy of -0.44 kJ/mol, but the ZPE corrections are nearly equal and opposite. Therefore \( sp \)(\( sp^3 \) synclinal interactions do not have a large effect, and \( sp \)(\( sp^3 \) synclinal and gauche interactions appear to be additive for nitriles. The electronic energy for ethynylcyclohexane predicts that the axial conformation [having two \( sp \) (\( sp^3 \) synclinal interactions] is preferred over the equatorial, but taking ZPE corrections into account, the calculations predict that the equatorial becomes more favorable. This outcome disagrees with what is predicted for acyclic compounds. The ZPE correction leads to the difference between axial and equatorial of 0.1kJ/mol (equatorial being more preferred). The most recent experimental A-value, which is based on \(^{13}\)C NMR in CFCl \(_3\) solution, is 2.16 ± 0.05 kJ/mol [8]. Despite qualitative agreement with the calculated value, the experimental A-value is much larger. The electronic energy for cyanocyclohexane predicts that the axial conformation [having two \( sp \)(\( sp^3 \) synclinal interactions] is preferred over the equatorial, and taking ZPE corrections into account, the calculations predict that the axial remains slightly more favorable. This outcome agrees with what is predicted for acyclic compounds but disagrees with the most recent experimental A-value is 0.90 ± 0.08 kJ/mol. [8] The solvents in which the A-values are measured in may possibly affect the values obtained relative to gas phase equilibria. This could explain the energy differences between calculations and experimental values for monosubstituted cyclohexanes. Dipole moments found using the 3-21G method for axial and equatorial conformations of ethynylcyclohexane and cyanocyclohexane show bigger dipole moments for equatorial. As a consequence, solvent may shift the equilibria for monosubstituted cyclohexanes toward the equatorial conformation.

ACKNOWLEDGMENTS

The authors are grateful to the students of Chem 122H (Fall 2010) for their work and calculations, and to Professor T.H. Morton for his guidance and advice.

REFERENCES