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At what chain length do unbranched alkanes prefer folded conformations?

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Short unbranched alkanes are known to prefer linear conformations, while long unbranched alkanes are folded. It is not known with certainty at what chain length the linear conformation is no longer the global minimum. To clarify this point, we use *ab initio* and density functional methods to compute the relative energies of the linear and hairpin alkane conformers for increasing chain lengths. Extensive electronic structure calculations are performed to obtain optimized geometries, harmonic frequencies and accurate single point energies for the selected alkane conformers from octane through octadecane. Benchmark CCSD(T)/cc-pVTZ single point calculations are performed for chains through tetradecane, while approximate methods are required for the longer chains up to octadecane. Using frozen natural orbitals to unambiguously truncate the virtual orbital space, we are able to compute composite CCSD FNO(T) single point energies for all the chain lengths. This approximate composite method has significant computational savings compared to full CCSD(T) while retaining ~ 0.15 kcal/mol accuracy compared to the benchmark results. More approximate dual-basis resolution-of-the-identity double-hybrid DFT calculations are also performed and shown to have reasonable 0.2 – 0.4 kcal/mol errors compared with our benchmark values. After including contributions from temperature dependent internal energy shifts, we find the preference for folded conformations to lie between hexadecane and octadecane, in excellent agreement with recent experiments [Lüttschwager, N. O.; Wassermann, T. N.; Mata, R. A.; Suhm, M. A. *Angew. Chem. Int. Ed.* 2013, 52, 463].

I. INTRODUCTION

Unbranched alkane chains (C_nH_{2n+2}) are of fundamental importance in organic chemistry. They are constituents of fossil fuels and polymers, as well as important structural motifs in lipids and other biomolecules. It is clearly important to understand their conformational and thermochemical properties.

The conformer potential energy surface of an unbranched alkane is characterized by torsional twists which lead from linear chains to highly deformed structures dominated by intramolecular dispersion forces. At temperatures less than 300 Kelvin, short alkanes ($n = 4 - 8$) in the gas phase are well known to prefer the linear all-trans ($T = 180^\circ$, $X = 90^\circ$ and $G = 60^\circ$ for trans, cross and gauche dihedral angles respectively) conformation. However, as the length of the alkane grows there must be a point where the attractive intramolecular interactions will cause the chain to self-solvate into a folded conformer. A cross-gauche-cross rotation combination ($T \dots XGX \dots T$) is sufficient to fold the chain,¹ but this creates an energetically unfavorable *syn*-pentane like conformation. In addition, the chain ends are not parallel in this conformation, reducing the possible stabilization due to van der Waals attraction. A hairpin conformation with four gauche rotations² ($T \dots GGTGG \dots T$) minimizes the number of strained bonds and allows an energetically favorable parallel arrangement of the chain ends, leading it to be the suggested global minimum for longer alkanes.²⁻⁴ These three conformational structures are illustrated in Figure 1.

It is well known that the computation of relative energies involving weak interactions presents a significant challenge for computational studies. In the case of short alkanes ($n = 4 - 6$), standard DFT methods are largely inadequate to describe the conformer energies and ordering of states⁵ while *ab initio* methods past second order perturbation theory are necessary for a full description of the more configurationally complicated transition state conformer structures.⁶ As the length of the alkane chain increases so does the importance of a proper

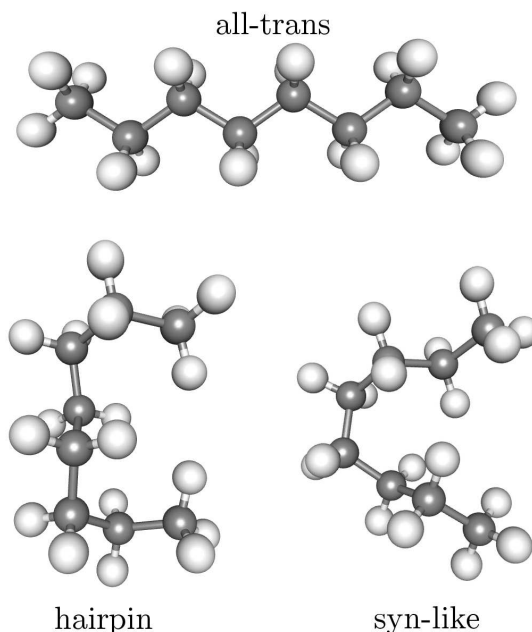


FIG. 1. Illustrative optimized alkane structures.

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treatment of dispersion.¹ In the case of octane ($n = 8$) second order perturbation theory calculations underestimate the “bowl” conformer (*GGTGG*) energy difference while coupled cluster theory (CCSD) will overestimate the energy difference by ~ 0.5 kcal/mol compared to the “gold standard” inclusion of perturbative triples obtained using CCSD(T).

With these computational difficulties in mind, it is clear why the hairpin conformer critical chain length (at which it becomes the global minimum) is difficult to determine accurately. Early work by Goodman² using force field and semi-empirical calculations suggested a turning point anywhere between $n = 12$ to $n = 26$, with subsequent force field calculations³ also pointing towards $n = 18$ as the critical chain length. This problem was experimentally addressed in the recent work of Lüttschwager *et al.*⁴ Their experiment used Raman spectroscopy with a supersonic jet expansion apparatus and concluded that the critical chain length is between $n = 16$ and $n = 18$ at temperatures of 100K. The accompanying theoretical work uses a local coupled cluster approach to also suggest a critical chain length of $n = 18$.

In this paper we will first obtain benchmark *ab initio* structures, electronic and harmonic vibrational energies for the linear (all-trans) and hairpin alkane conformers of increasing length starting with octane ($n = 8$) through tetradecane ($n = 14$). These benchmark values will be used to characterize various approximate methods that are extendable to longer chains ($n > 14$) with which we predict the critical alkane chain length. Although they are not the focus of this study, entropic effects become important as the temperature increases, and this is discussed briefly in the conclusions.

II. ELECTRONIC STRUCTURE CALCULATIONS

We perform *ab initio* and DFT electronic structure calculations on the n -alkane ($n = 8, 10 - 18$) linear and hairpin conformers using the GAMESS^{7,8} and ACES III⁹ quantum chemistry packages running on the University of Florida HPC, HiPerGator and University of Connecticut BECAT clusters. All calculations in this work use Dunning’s correlation consistent family of basis sets (cc-pVnZ, $n=T, Q$).¹⁰ For resolution-of-the-identity calculations the triple-zeta fitting basis set of Weigend *et al.*¹¹ (cc-pVTZ-RI) are used in conjunction with the standard cc-pVTZ basis set. Unless explicitly stated all correlation calculations in this work assume the frozen-core approximation where all $1s$ carbon orbitals are dropped from the correlation space while the corresponding last virtual orbital is retained.

For shorter ($n = 2 - 7$) alkane chains it has been shown^{5,6,12} that the quality of the final optimized geometry is more strongly dependent on the level of the correlation theory than on the basis set. Additional tests show that including correlation beyond that of second or-

der Møller-Plesset perturbation theory (MP2) is unnecessary. For the longer alkane species we find that the use of a small basis set (such as the Pople split valence 6-311G* basis set) that has insufficient polarization functions will lead to erroneous hairpin structures. Therefore geometry optimizations of the alkane conformers used in this work are obtained using the MP2 level of theory (with analytic gradients) and the cc-pVTZ basis set. Harmonic zero point energy (ZPE) shifts are computed numerically using analytic first derivatives at the MP2/cc-pVTZ all-electron level of theory. Due to the cost of numerical MP2 Hessians, the massively parallel ACES III program is used to perform the necessary first derivatives with the caveat that only all-electron MP2 gradients are available. This change of theory between geometries and hessian is found to introduce a negligible error of 0.03 kcal/mol when considering relative conformer ZPE shifts.

High level single point energy calculations are computed using coupled cluster theory with singles, doubles, and perturbative triples¹³⁻¹⁵ (CCSD(T)) and the cc-pVTZ basis set. Higher order effects such as contributions from the core-valence correlation energy or higher order excitations (full triples, quadruples etc.) are not included as their effects are small and cancel nearly identically in conformational energy differences. It is convenient to analyze the calculated energies by orders of perturbation theory. In this way the MP2 correlation energy is given by $\Delta_{\text{MP2}} = E(\text{MP2}) - E(\text{SCF})$, while higher order contributions can be conveniently given as $\Delta_{\text{CCSD}} = E(\text{CCSD}) - E(\text{MP2})$, $\Delta_{\text{CCSD(T)}} = E(\text{CCSD(T)}) - E(\text{MP2})$, and $\Delta(\text{T}) = E(\text{CCSD(T)}) - E(\text{CCSD})$. Because the basis set convergence of the post-MP2 correlation is much faster than the second order contribution¹⁶, we can estimate the effects of going to the complete basis set (CBS) limit by combining large basis MP2 energies and small basis coupled cluster correlation energies. Using the cc-pVTZ and cc-pVQZ basis sets, we separately extrapolate the SCF and MP2 correlation energy using the linear extrapolation formulas of Schwenke¹⁷

$$E_{\infty}(\text{SCF}) = E_{n-1}(\text{SCF}) + F_{n-1,n}(E_n(\text{SCF}) - E_{n-1}(\text{SCF})) \quad (1)$$

(with $F_{3,4} = 1.3071269$) and Helgaker *et al.*¹⁸

$$\Delta_{\infty}\text{MP2} = \frac{n^3\Delta_n\text{MP2} - (n-1)^3\Delta_{n-1}\text{MP2}}{n^3 - (n-1)^3} \quad (2)$$

respectively. Here $E_n(\text{SCF})$ and $\Delta_n\text{MP2}$ refers to the SCF and MP2 correlation energy computed with the cc-pVnZ basis set. Adding in the coupled cluster correlation energy to form a composite CBS energy

$$E(\text{CCSD(T)})/\text{CBS} = E_{\infty}(\text{SCF}) + \Delta_{\infty}\text{MP2} + \Delta_{\text{CCSD(T)}} \quad (3)$$

we obtain a 0.2 kcal/mol shift compared to the CCSD(T)/cc-pVTZ relative energy for the $n = 8 - 14$ alkanes (see Table I). As the cost of doing an MP2/cc-pVQZ calculation for the alkane chains longer than $n = 14$ starts to become prohibitively expensive (over 1800

TABLE I. Benchmark *ab initio* conformer energy differences (hairpin – linear, in kcal/mol) for the $n = 8 - 14$ alkane chains. Harmonic ZPE energies were computed at the MP2/cc-pVTZ level of theory.

Method	C ₈ H ₁₈	C ₁₀ H ₂₂	C ₁₂ H ₂₆	C ₁₄ H ₃₀
cc-pVTZ				
SCF	5.19	5.50	5.88	9.76
ΔMP2	-4.10	-4.76	-5.59	-10.47
ΔCCSD	0.83	1.00	1.18	2.11
Δ(T)	-0.49	-0.58	-0.70	-1.41
ZPE	0.58	0.60	0.58	0.69
cc-pVQZ				
SCF	5.24	5.56	5.95	9.89
ΔMP2	-4.07	-4.70	-5.52	-10.50
CCSD(T)	1.44	1.18	0.79	0.03
CCSD(T)/CBS	1.57	1.36	0.99	0.14

basis functions and 130 electrons) we instead omit the CBS correction and include a 0.2 kcal/mol error estimate in our final result.

Using the massively parallel ACES III program allowed us to compute the CCSD energies for all the alkane chain lengths considered here. However the $O(o^3v^4)$ (for o occupied and v virtual orbitals) scaling of the perturbative triples quickly becomes problematic. With our available computational resources the perturbative triples contribution could be computed only for alkane chains up to $n = 14$. In order to alleviate the cost of including triples it is possible to truncate the virtual space by some amount p , providing a p^4 prefactor which can enable larger calculations to be done. To do so systematically and unambiguously we use the frozen natural orbital (FNO) method^{19,20} which uses the MP2 density matrix to make new virtual orbitals. The Hartree-Fock virtual orbitals can then be replaced with the appropriately transformed MP2 virtual natural orbitals, resulting in a set of virtual orbitals sorted by their contribution to the correlation energy. The virtual space can then be truncated by examining the MP2 virtual occupation numbers (eigenvalues of the MP2 density matrix) and dropping orbitals with an occupation smaller than some predetermined threshold. In this work we take a threshold of 1×10^{-4} , which results in 40% of the virtual orbitals being dropped (a prefactor p^4 of 0.13). Additional savings are also realized in the form of memory storage and data communication requirements.

There are a variety of ways to get a final FNO coupled cluster energy. Two composite energy schemes are considered:

$$E(\text{FNO CCSD(T)}) = E(\text{MP2}) + \Delta_{\text{FNO}}\text{CCSD(T)} \quad (4)$$

and

$$E(\text{CCSD FNO(T)}) = E(\text{CCSD}) + \Delta_{\text{FNO}}(\text{T}). \quad (5)$$

both of which have comparable accuracies for smaller systems (see Table II). We choose to use the latter composite

method (Equation 5), which makes approximations only in the triples calculation. Our particular implementation in GAMESS and ACES III uses the converged T_1 and T_2 amplitudes from an $\Delta_{\text{FNO}}\text{CCSD}$ calculation to compute the perturbative triples contribution. The error associated with using these amplitudes compared to complete virtual space CCSD amplitudes which are then truncated by the FNO prescription is small.²¹ Similar composite methods have been used by DePrince and Sherrill with comparable accuracy obtained.²¹

An approximate theoretical method that scales better than the usual CCSD $O(o^2v^4)$ calculation with very reasonable accuracy for short alkanes⁵ is double-hybrid density functional theory^{22,23} (DH-DFT). This method mixes SCF and DFT exchange with DFT and MP2 correlation energy then corrects the dispersion energy empirically using Grimme’s D3 correction.²⁴ To facilitate calculations of even larger molecules, we have recently implemented²⁵ in GAMESS the dual-basis^{26–30} SCF method. Here the SCF energy is approximated by a converged small (truncated) basis energy calculation. The large (with polarization functions) basis contribution is then approximated by a single new Fock matrix constructed from the projected small basis density matrix. This approximate SCF method is much faster than a full SCF calculation with errors comparable to standard density-fitted SCF methods. We evaluate the DH-DFT method in GAMESS using dual-basis DFT married with the resolution-of-the-identity³¹ MP2 method (referred together with the dual-basis SCF to as DB-RI), a further approximation³² that adds trivial errors while shifting all of the leading computational cost to the single large basis Fock matrix build.

III. COMPUTATIONAL RESULTS AND DISCUSSION

When computing relative conformer energies for short ($n \leq 6$) alkane chains, values taken from MP2 level calculations are sufficient to give 0.15 kcal/mol RMS accuracy⁵ (taking CCSD(T) values as the correlation benchmark). Even for more demanding structures such as transition states (pentane⁶ for example) an RMS of 0.2 kcal/mol is quite satisfactory for many purposes. Post MP2 contributions to the correlation energy at the CCSD level provide a noticeable improvement for transition states, though there is a tendency for it to overcompensate by 0.2 – 0.5 kcal/mol for more strongly rotated hexane conformers. The additional correlation energy coming from perturbative triples is consistent with calculations performed on systems with dispersion dominated interactions.^{33,34}

With our available computing resources we are able to compute accurate *ab initio* coupled cluster conformer energies (CCSD(T)/cc-pVTZ) for the alkane chains $n = 8 - 14$, requiring 25,000 CPU hours for each $n = 12$ conformer and 65,000 CPU hours for each $n = 14$ conformer

TABLE II. Computed *ab initio* conformer energy differences (hairpin – linear, in kcal/mol) for the $n = 8 - 18$ alkane chains using the cc-pVTZ basis set. Both FNO composite energies are shown, as well as the temperature dependent enthalpy changes.

Method	C ₈ H ₁₈	C ₁₀ H ₂₂	C ₁₂ H ₂₆	C ₁₄ H ₃₀	C ₁₆ H ₃₄	C ₁₈ H ₃₈
SCF	5.19	5.50	5.88	9.76	10.11	11.06
Δ MP2	-4.10	-4.76	-5.59	-10.47	-11.70	-13.77
Δ CCSD	0.83	1.00	1.18	2.11	2.34	2.75
Δ_{FNO} MP2	-3.80	-4.32	-5.09	-9.62	-10.71	-12.61
Δ_{FNO} CCSD	-0.13	0.94	1.16	2.05	2.27	2.66
Δ_{FNO} (T)	-0.59	-0.49	-0.59	-1.23	-1.39	-1.64
CCSD FNO(T)	1.51	1.25	0.89	0.18	-0.63	-1.60
FNO CCSD(T)	1.50	1.20	0.86	0.12	-0.70	-1.69
ΔH_{0K}	2.09	1.85	1.47	0.86	0.05	-0.92
ΔH_{100K}	2.02	1.76	1.37	0.67	-0.14	-1.11
ΔH_{298K}	1.78	1.51	1.11	0.35	-0.46	-1.43

(see Figure 2. Obtaining accurate values for this wide range of chain lengths allows us to benchmark any further approximate methods that we choose to use in order to extend our analysis to longer alkane chains. The breakdown of the post SCF correlation contributions through CCSD(T) for these medium length alkanes can be found in Table I. Two systematic trends can be noticed here: the MP2 conformer energy consistently underestimates by 0.5 kcal/mol while the CCSD energy overshoots by 0.5 kcal/mol, causing the correct value to fall directly in between the two values.³⁵ This illustrates the size of both infinite order singles and doubles, providing a much more complete dispersion contribution, and the significant role of connected triples in these extended systems.

As mentioned earlier, while we are able to perform CCSD energy calculations for all the chain lengths under consideration, the $O(o^3v^4)$ cost of the perturbative triples becomes untenable for chains longer than $n = 14$ on available computational resources. Therefore we opted for an approximate treatment using the CCSD FNO(T) virtual space truncation scheme.^{19,20} Numerical tests show that an occupation number threshold of 1×10^{-4} is sufficient to drop approximately 40% of the virtual space while retaining ~ 0.1 kcal/mol accuracy compared to the full virtual space result, as illustrated in Table II. Because of the size extensivity of these many-body methods this error grows very slowly with the number of electrons, reaching 0.15 kcal/mol at chain lengths of $n = 14$. A beneficial cancellation of error can be observed here where the FNO composite method predicts conformer energies between that of the CCSD(T) value and the CCSD(T)/CBS extrapolated CBS estimate. Because of computational cost considerations we include this ± 0.2 kcal/mol variance within the error estimate of the relative conformer energies.

We compute the harmonic ZPE of the shorter alkane chains ($n = 8 - 14$) at the all-electron MP2 level of theory, with the results presented in Table I. Thermodynamic considerations are taken into account by computing the change in internal energy (vibration, rotation and translation) as a function of temperature. The increase in

number of degrees of freedom as the chains lengthen significantly increases the computational cost, necessitating an approximate ZPE shift for the longer alkanes. Our final CCSD FNO(T) relative conformer energies with ZPE and temperature dependent shifts (simply referred to as ΔH) are given in Table II. Noting the nearly constant ZPE and temperature shift in ΔH for each of the shorter alkanes, we take as an approximation that the ΔH shift for the longer ($n > 14$) alkanes is the same as for the $n = 14$ alkane. Because of this added approximation to the final relative conformer energy we increase the estimated error bars to 0.3 kcal/mol for the longer

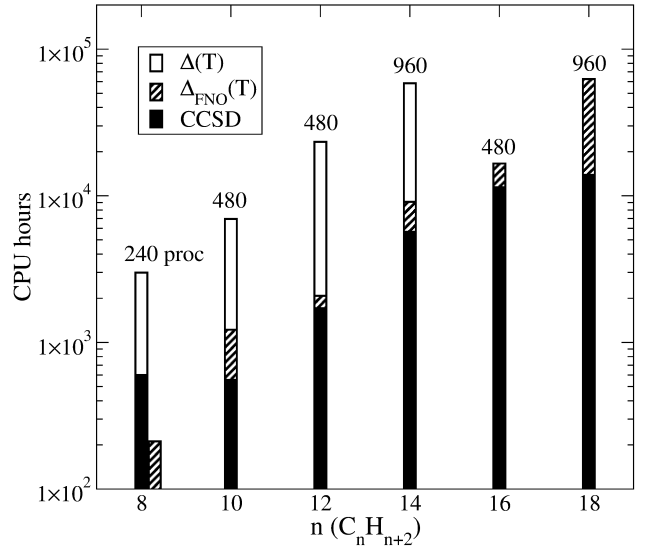


FIG. 2. Total CPU hours used to compute the correlation energy for a single alkane conformer. Also listed above each timing bar is the number of processors used. Calculations for the $n = 8 - 12$ and $n = 16$ chains were performed on the HPC cluster while the $n = 14$ and $n = 18$ chain calculations were performed on the new HiPerGator cluster. The difference between clusters being the increased number of available processors and inter-node communication bandwidth.

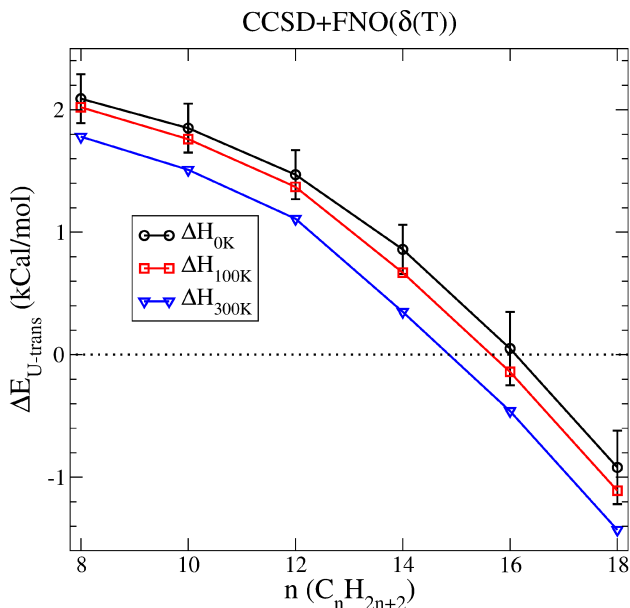


FIG. 3. Calculated enthalpy differences, $\Delta H = \Delta H_{\text{hairpin}} - \Delta H_{\text{linear}}$, using CCSD FNO(T)/cc-pVTZ single point energies and MP2/cc-pVTZ harmonic vibrational frequencies including temperature dependent shifts.

alkane chains. Our final ΔH values (plotted in Figure 3) show that the $n = 18$ alkane chain the hairpin conformer is definitely preferred over the linear structure by a full kcal/mol. For low temperatures ($0 \sim 100$ K) the $n = 16$ hairpin conformer is possibly preferred with the estimated error bars extending on either side of the 0 line, however as the temperature increases our ΔH_{300K} value strongly suggests that the $n = 16$ hairpin is preferred. These results are in complete agreement with the gas jet experimental (performed at 100K) work of Lüttschwager *et al.*⁴ where the hairpin preference is found to be between $n = 16$ and 18.

With the FNO coupled cluster calculations costing 12% of the corresponding full virtual space calculations, we were able to perform CCSD FNO(T) calculations for all the alkane chains through $n = 18$. Even so, the $O(o^3 v^4)$ scaling remains such that the $n = 18$ chain required 60,000 CPU hours for each conformer to obtain the relative energy. Clearly the attractiveness of an approximate theory with a reduced computational scaling is great. Qualitatively some force field and semi-empirical calculations perform well, with OPLS-AA³ and MM2² both predicting that the $n = 18$ conformer energetically prefers the hairpin with PM3 predicting $n = 12$ (this is excluding ZPE and other thermodynamic shifts). However other commonly used force field methods do not perform as well such as MM3 and AMBER, which predict² the hairpin turning point at $n = 25$ and $n = 26$ respectively. Taking advantage of the polymer like repetitive structure of the long alkanes Lüttschwager *et al.* have performed a composite local coupled cluster (local-CC) correlation calculation for the $n = 14 - 22$ series, includ-

ing ZPE and thermal shifts, and compute that $n = 18$ is the first lowest energy hairpin length. Qualitatively this is in good agreement with our own results, though quantitatively we find the local-CC results to be too high compared to our CCSD FNO(T) values, but very consistent with the DH-DFT results (see Table III and Figure 4).

Density functional theory is not typically a good choice for non-covalently bonded and weakly interacting conformer studies (or any system where dispersion is an important consideration). However with the inclusion of London type dispersion³⁶ through an empirically derived additive correction (in this case using Grimme's -D3 function²⁴) DFT methods can be quantitative^{5,37-39} within the limits of the training set. In our previous work²⁵ the accuracy of the B2-PLYP²², B2GP-PLYP⁴⁰ and DSD-BLYP⁴¹ double-hybrid DFT composite functionals using the dual-basis²⁷ resolution-of-the-identity³¹ approximation (see the previous methods section) were tested for a variety of non-covalently bonded dimers and small alkane conformers (so called S22⁴² and ACONF⁵ test set). The results of which were promising, with an average RMS error of 0.5 kcal/mol for the S22 set and 0.1 kcal/mol for the $n = 4 - 7$ alkanes. Using these DH-DFT/DB-RI-MP2 composite methods, we return to the hairpin preference problem at hand and compute relative conformer energies for all the long alkanes ($n = 8 - 18$) and compare the resulting values to our CCSD FNO(T) values in Table III. As can be seen in Figure 4 the DH-DFT/DB-RI-MP2 conformer energies track the higher level *ab initio* results very well, the best curve coming from the DSD-BLYP functional with a nearly constant 0.1 kcal/mol error. With a computational cost many orders less than the predictive CCSD FNO(T) composite method considered here, these DH-DFT/DB-RI-MP2 composite methods continue to be a promising approximate method in cases too computationally difficult for coupled cluster calculations.

IV. SUMMARY AND CONCLUSIONS

As the length of unbranched alkane chains reaches some critical length, intramolecular dispersion forces cause a self-solvation effect in which the chains assume a folded conformation. To accurately determine this critical chain length, linear and hairpin alkane conformer structures were optimized using the MP2/cc-pVTZ level of theory for chains of length up through $n = 18$. Benchmark CCSD(T)/cc-pVTZ single point energy calculations were then performed for octane through tetradecane using the ACES III⁹ massively parallel quantum chemistry package. Harmonic zero point energies and temperature shifts were computed using the MP2/cc-pVTZ level of theory.

For chains longer than $n = 14$ it was necessary to use more approximate methods to obtain conformer energy differences. It was found that our CCSD FNO(T)

TABLE III. Relative conformer energies (hairpin – linear, in kcal/mol) for the $n = 8 - 18$ alkane chains computed using various composite methods with the cc-pVTZ basis set. Also shown are the local-CC values from Lüttchwager *et al.*⁴ Benchmark CCSD(T) energies are included for available chain lengths. Here * denotes the reported hairpin/linear crossing.

Method	C ₈ H ₁₈	C ₁₀ H ₂₂	C ₁₂ H ₂₆	C ₁₄ H ₃₀	C ₁₆ H ₃₄	C ₁₈ H ₃₈
CCSD(T)	1.44	1.18	0.79	0.03		
CCSD FNO(T)	1.51	1.25	0.89	0.18	-0.63	-1.60
B2-PLYP-D3/DB-RI	1.79	1.55	1.17	0.47	-0.39	-1.38
B2GP-PLYP-D3/DB-RI	1.81	1.59	1.25	0.71	-0.10	-1.03
DSD-BLYP-D3/DB-RI	1.65	1.40	1.03	0.35	-0.49	-1.49
local-CC ⁴				0.73	-0.04	-1.09
OPLS-AA ³					2.2[-1]	1.3[-1]
MM2 ²						*
PM3 ²				*		

method which takes the full CCSD correlation energy and adds the perturbative triples correlation energy taken from a frozen natural orbital calculation where retaining only 60% of the virtual space is required to obtain results comparable to full CCSD(T) results (Table II). We have also explored the effectiveness of the dual-basis resolution-of-the-identity double-hybrid density functional theory approach to this problem. With a computational cost several orders of magnitude less than the more rigorous *ab initio* methods considered here we find that these approximate DFT methods performed well with errors ~ 0.2 kcal/mol.

Computing the conformer temperature enthalpy differences using the CCSD FNO(T) electronic energies and approximate MP2/cc-pVTZ ZPE shift for alkane chains up through $n = 18$ show that the temperature dependent hairpin preference takes place at $n \geq 16$, with a confidence of ~ 0.3 kcal/mol. This finding is in complete agreement with the experimental results of

Lüttchwager *et al.*⁴

As the temperature increases, entropic effects will become important. The Gibbs free energy difference between linear and folded chains will tend to decrease due to the increased entropy of the folded conformation. An accurate assessment of this effect would require conformational sampling of the CCSD(T) energy surface, a calculation that greatly exceeds the computational resources available to us. However, the close agreement of our calculated results with the low temperature results of Lüttchwager *et al.*⁴ suggests that our conclusions would be significantly altered by entropic effects only at much higher temperatures.

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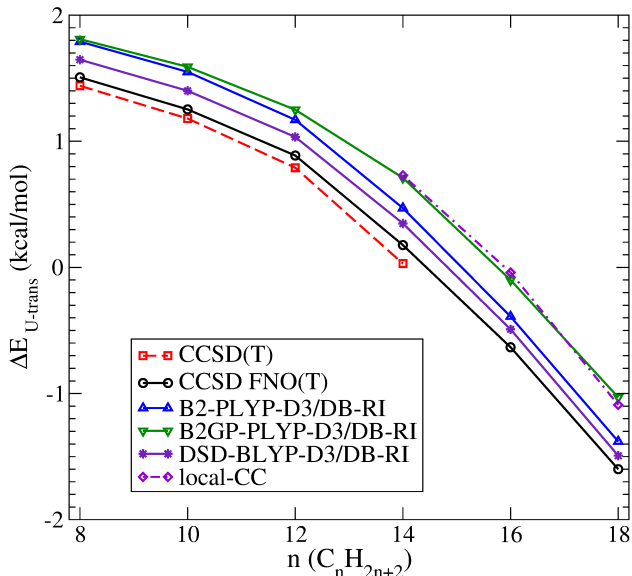


FIG. 4. Composite relative single point energies, $E_{\text{hairpin}} - E_{\text{linear}}$, compared against benchmark CCSD(T)/cc-pVTZ values.

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