

# Ab Initio vs Molecular Mechanics Thermochemistry: Homocubanes

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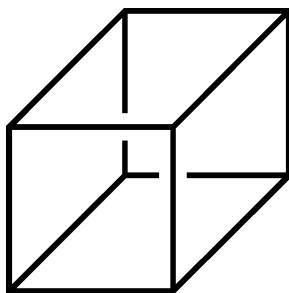
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The standard enthalpies of formation and strain energies for a series of homocubanes have been investigated by high-level ab initio G3(MP2)/B3LYP method. The relative stabilities of isomers are discussed. The comparison is made between the results of ab initio and molecular mechanics methods with the aim of assessing their performances. The usefulness of high-level calculations for generating thermochemical databases of relatively large molecules (e.g. C<sub>11</sub>H<sub>14</sub>) was also demonstrated.

## INTRODUCTION

The saturated polycyclic “cage” molecules such as homocubanes are interesting because their carbon skeletons often possess considerable strain energies (SE). This strain is manifested through long CC bonds, CCC angles which deviate significantly from the tetrahedral 109.5° value, and large positive standard enthalpies of formation.<sup>1</sup>

The purpose of this work was severalfold. First, we aim to provide accurate standard  $\Delta H_f^0$  values for a series of homocubanes for which no experimental data are currently available in the standard thermochemical database.<sup>2</sup> Second, the existing databases<sup>3</sup> and published reports<sup>4,5</sup> for saturated polycyclic hydrocarbons rely on molecular mechanics (MM) methods whose accuracy for this class of compounds needs to be better established. The comparison of MM results with the results of high-level ab initio calculations is thus necessary to validate the reliability of the former. Third, in the experimental thermochemical studies<sup>6,7</sup> of cage hydrocarbons, the reliability of wholesale application of MM methods to such compounds was cast in some doubt.<sup>6,7</sup> We have therefore performed high-level ab initio thermochemical calculations for a series of homocubanes **1–20** whose structural formulas are shown in Chart 1. The homocubanes are derivatives of cubane



in which one or more of the edges had been replaced by methylene bridges.

## METHOD OF CALCULATION

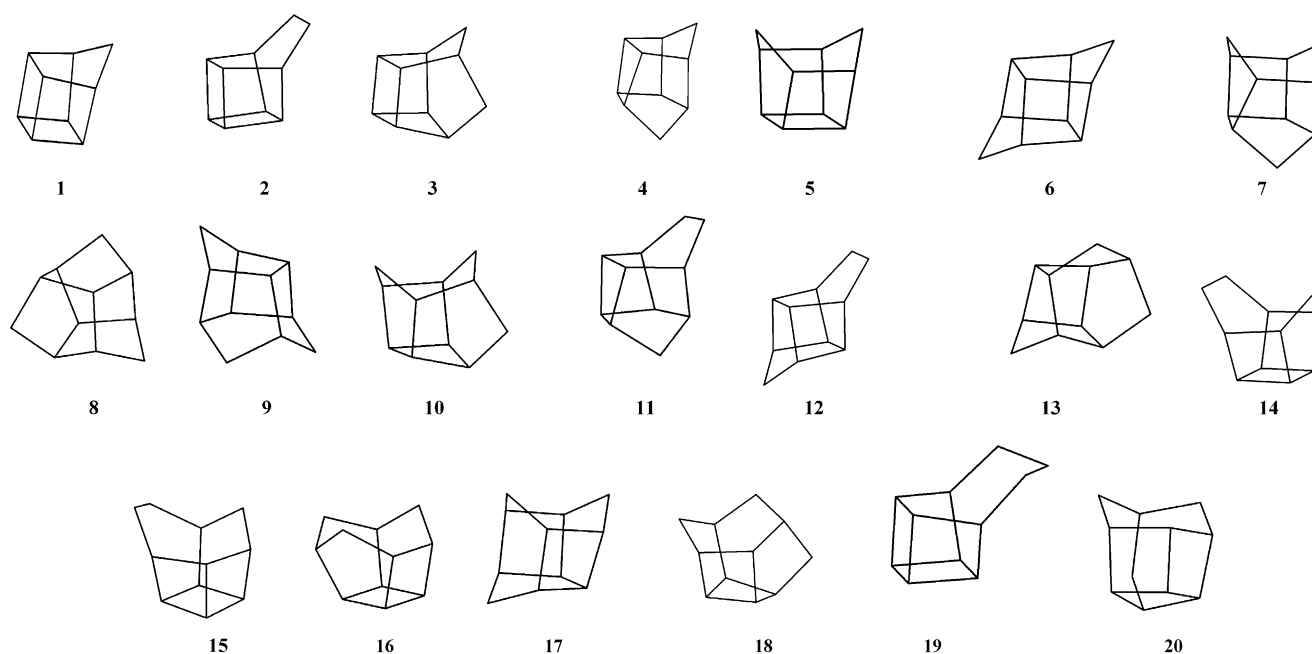
The ab initio calculations were performed with Gaussian-03W software<sup>8</sup> using G3(MP2)/B3LYP method. The method

has typical precision for calculating  $\Delta H_f^0$ (298 K) of hydrocarbons which is around  $\pm 3$  kJ mol<sup>-1</sup> ( $\pm 0.75$  kcal/mol) and is therefore often used in accurate thermochemical calculations.<sup>9</sup> The reason for selecting the G3(MP2)/B3LYP method, rather than the original G3 method, lies in computational tractability. The size of homocubane molecules (and the number of basis functions required for such calculations) was too large for successful G3 calculation. G3(MP2)/B3LYP provides total electron energies from which accurate standard enthalpies can be deduced for a wide range of organic compounds using hypothetical reactions of isodesmic, isomerization, or atomization type. All the molecular structures obtained in this work represent true minima on the potential energy surface as is indicated by the absence of imaginary harmonic frequencies. The selection of “anchor” compounds in isodesmic reactions was made so that only those with accurate and reliable enthalpies were included. The experimental gas phase  $\Delta H_f^0$ (298 K) values for the “anchor compounds” were as follows: C<sub>2</sub>H<sub>6</sub> (−83.8 kJ mol<sup>-1</sup>), cubane (622.2 kJ mol<sup>-1</sup>), CH<sub>4</sub> (−74.87 kJ mol<sup>-1</sup>), CH<sub>3</sub>CH<sub>2</sub>CH<sub>3</sub> (−104.7 kJ mol<sup>-1</sup>), CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> (−125.6 kJ mol<sup>-1</sup>), CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> (−146.8 kJ mol<sup>-1</sup>), (CH<sub>3</sub>)<sub>3</sub>CH (−134.2 kJ mol<sup>-1</sup>). These are the most accurate values available at present.<sup>2</sup> It should be mentioned at this point that even the experimental enthalpy of formation for cubane itself is not beyond doubt. One may recall the discrepancy of the order of 12 kJ/mol which was reported for dimethyl cubane-1,4-dicarboxylate.<sup>10,11</sup> Such discrepancies indicate that considerable experimental difficulties are encountered when measuring enthalpies. It therefore becomes necessary to resort to high-level calculations as the most reliable source of enthalpies currently available.

Ab initio calculations for the title molecules are feasible on a standard Pentium PC which makes them suitable for database generation. This was demonstrated in this work in which each calculation was performed on PC with Pentium 4 chip (single CPU, 3 GHz clock-speed, 1GB RAM, 36GB hard disk space) under Windows 2000 operating system. The wall-clock time for the longest calculations at G3(MP2)/B3LYP level was 22.8 h. Essentially, each calculation involves full geometry optimization at 6-31G\* level followed by the G3 sequence of calculations.<sup>9</sup> After that an additional step was performed which comprised a single point frequency

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Chart 1



1	Pentacyclo [4.3.0.0 <sup>2,5</sup> .0 <sup>3,8</sup> 0 <sup>4,7</sup> ]nonane
2	Pentacyclo [4.4.0.0 <sup>2,5</sup> .0 <sup>3,8</sup> 0 <sup>4,7</sup> ]decane
3	Pentacyclo [4.4.0.0 <sup>2,5</sup> .0 <sup>3,9</sup> 0 <sup>4,7</sup> ]decane
4	Pentacyclo [5.3.0.0 <sup>2,5</sup> .0 <sup>3,9</sup> 0 <sup>4,8</sup> ]decane
5	Pentacyclo [4.4.0.0 <sup>2,5</sup> .0 <sup>3,9</sup> 0 <sup>4,8</sup> ]decane
6	Pentacyclo [5.3.0.0 <sup>2,6</sup> .0 <sup>3,9</sup> 0 <sup>4,8</sup> ]decane
7	Pentacyclo [5.4.0.0 <sup>2,6</sup> .0 <sup>3,10</sup> 0 <sup>5,9</sup> ]undecane
8	Pentacyclo [6.3.0.0 <sup>2,6</sup> .0 <sup>3,10</sup> 0 <sup>5,9</sup> ]undecane
9	Pentacyclo [5.4.0.0 <sup>2,6</sup> .0 <sup>3,10</sup> 0 <sup>4,8</sup> ]undecane
10	Pentacyclo [5.4.0.0 <sup>2,6</sup> .0 <sup>3,10</sup> 0 <sup>5,8</sup> ]undecane
11	Pentacyclo [5.4.0.0 <sup>2,5</sup> .0 <sup>3,11</sup> 0 <sup>4,8</sup> ]undecane
12	Pentacyclo [5.4.0.0 <sup>2,6</sup> .0 <sup>3,9</sup> 0 <sup>4,8</sup> ]undecane
13	Pentacyclo [5.4.0.0 <sup>2,5</sup> .0 <sup>3,10</sup> 0 <sup>4,8</sup> ]undecane
14	Pentacyclo [5.4.0.0 <sup>2,6</sup> .0 <sup>3,11</sup> 0 <sup>4,10</sup> ]undecane
15	Pentacyclo [5.4.0.0 <sup>2,10</sup> .0 <sup>5,9</sup> 0 <sup>8,11</sup> ]undecane
16	Pentacyclo [5.4.0.0 <sup>3,10</sup> .0 <sup>5,9</sup> 0 <sup>8,11</sup> ]undecane
17	Pentacyclo [5.4.0.0 <sup>2,6</sup> .0 <sup>3,10</sup> 0 <sup>4,9</sup> ]undecane
18	Pentacyclo [5.4.0.0 <sup>2,5</sup> .0 <sup>3,11</sup> 0 <sup>4,9</sup> ]undecane
19	Pentacyclo [5.4.0.0 <sup>2,10</sup> .0 <sup>3,9</sup> 0 <sup>8,11</sup> ]undecane
20	Pentacyclo [5.3.1.0 <sup>2,5</sup> .0 <sup>3,10</sup> 0 <sup>4,9</sup> ]undecane

calculation. The purpose of this additional step was to confirm the existence of true minimum via the absence of imaginary vibrational frequencies. We have also performed the same calculations on a PC with lower CPU clock speed

(1.8G Hz) and time taken was 42 h. Obviously, the timings are inversely proportional to the clock-speeds. The timings given were for the longest calculations, and they concerned the largest molecules i.e., trishomocubanes (C<sub>11</sub>H<sub>14</sub>). For

**Table 1.** Standard Enthalpies of Formation  $\Delta H_f^0$  (g, 298.15 K)/kJ mol<sup>-1</sup> and Strain Energies SE/kJmol<sup>-1</sup> for Cubane and Homocubanes **1–20**<sup>a</sup> Obtained by G3B3LYP (G3) and Molecular Mechanics (MM) Calculations<sup>b</sup>

molecule	(no. of four-member rings present)	$\Delta H_f^0$ (G3) <i>isod</i> ( <i>atom</i> )	SE (G3)	$\Delta H_f^0$ (MM) <sup>3,4</sup>	SE (MM) <sup>3,4</sup>	$\Delta H_f^0$ (exp)/kJ mol <sup>-1</sup>
cubane	(6)	616.3(608.0)	684.3	622.8	695.0	622.2 ± 4.2
<b>1</b>	(4)	396.2(387.7)	485.1	397.9	494.3	
<b>2</b>	(4)	365.3(356.5)	475.1	350.5*	471.0	
<b>3</b>	(3)	276.8(268.1)	386.6	272.5	392.9	
<b>4</b>	(2)	198.6(189.9)	308.4	200.2	320.6*	
<b>5</b>	(3)	262.8(254.1)	372.6	256.7	377.1	
<b>6</b>	(2)	193.9(185.2)	303.7	186.4	306.8	
<b>7</b>	(1)	76.6 (67.7)	207.3	82.1* (86.5) <sup>6</sup>	218.8*	71.7 ± 5.0
<b>8</b>	(0)	35.2 (26.4)	165.9	39.2	176.0	
<b>9</b>	(1)	95.7 (86.9)	226.4	99.1	236.6	
<b>10</b>	(2)	149.8(141.0)	280.5	141.9	278.6	
<b>11</b>	(2)	168.7(159.9)	299.4	171.5 (161.9) <sup>2</sup>	308.2	
<b>12</b>	(2)	179.4(170.6)	310.1	201.8*	338.5*	
<b>13</b>	(1)	74.7 (66.0)	205.4	78.7	215.4	
<b>14</b>	(3)	244.1(235.3)	374.8	225.6*	362.3*	
<b>15</b>	(3)	248.9(240.1)	379.6	242.8	379.6	
<b>16</b>	(2)	154.1(145.3)	284.8	138.8*	275.5*	
<b>17</b>	(2)	130.4(121.6)	261.1	133.1	269.8	
<b>18</b>	(2)	189.7(180.9)	320.4	181.4	318.1	
<b>19</b>	(4)	354.5(345.7)	485.5	357.0 (339.3) <sup>2</sup>	493.8	
<b>20</b>	(3)	206.2(197.4)	336.9			

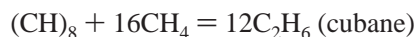
<sup>a</sup> *isod* and *atom* indicate the values obtained via isodesmic and atomization schemes, respectively. <sup>b</sup> References 2 and 3.

bishomocubanes, the completion times were shorter e.g. around 14 h on a 3 GHz machine.

## RESULTS AND DISCUSSION

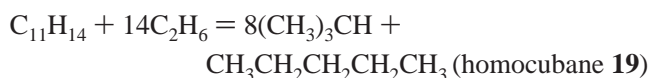
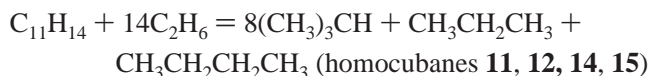
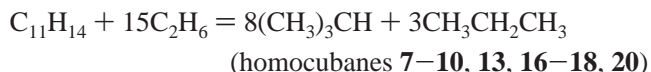
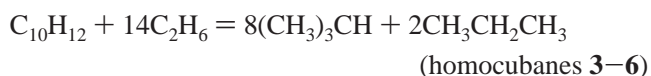
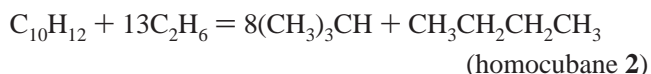
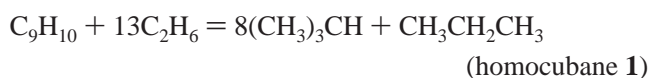
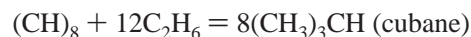
Selection of isodesmic reactions or anchors is not generally unique so we have also calculated enthalpies using atomization reactions in order to provide a cross check on isodesmic values. The standard enthalpies of formation of elements have been taken from the NIST source.<sup>2</sup> The comparison of isodesmic with atomization methods for calculating enthalpies suggests that the isodesmic method provides more accurate values.<sup>12</sup> This is due to the cancellation of errors in isodesmic reactions. Thus the enthalpy values used to discuss strain energies of homocubanes shall be those obtained via isodesmic reactions.

The following isodesmic reactions (at 298 K) were used for calculating enthalpies of formation in homocubanes:



Each isodesmic reaction included “anchor compounds”, with measured  $\Delta H_f$ (298 K) and a single compound whose  $\Delta H_f$  (298 K) needed to be calculated. Enthalpy change in an isodesmic reaction is given as  $\Delta H_r(298 \text{ K}) = \sum E_{\text{prod}} - \sum E_{\text{react}}$  where  $E$  refers to the total energies (including vibrational and rotational energy contributions at 298 K) obtained from G3/B3LYP calculations. Subsequently, the unknown  $\Delta H_f$  (298 K) was calculated from the known  $\Delta H_r$  and  $\Delta H_f$ (298 K) of the “anchor compounds”. The absolute enthalpies thus obtained are presented in Table 1 together with the enthalpies calculated via the atomization schemes.

The strain energies (SE) were calculated by using group equivalent reactions as described by Bachrach.<sup>13</sup> The reactions used were as follows:



Comparison of values listed in Table 1 suggests that enthalpy and strain energy are linearly correlated (correlation coeff = 0.996; STD = 10.28) and therefore the principal factor which determines the enthalpy in homocubanes can be considered to be steric strain. The enthalpy/strain depends, on the other hand, on the number of four-member/cyclobutane rings present in the molecule's structure. Thus cubane with 6 such rings has a very large strain energy (684.3 kJ/mol), while **8** without such rings has the lowest strain energy within the homocubane group (165.9 kJ/mol). The strains of individual rings are not additive. For instance, using SE in cubane and **8** we can calculate strain energies/ring for individual four-member and five-member rings as 86.4 and

27.7 kJ/mol, respectively. However, when adding individual ring strain energies in e.g. **1** we find that the strain energy obtained by ring addition (401 kJ/mol) differs considerably from the actual strain energy (485.1 kJ/mol, Table 1). One of the few available experimental thermochemical results available for large "cage" molecules supports this conclusion regarding nonadditivity.<sup>6</sup> The nonadditivity can be easily rationalized by noting that most four- and five-member rings in homocubanes are puckered, as the optimized homocubane structures in Chart 1 indicate. Ring puckering of course serves to reduce strain energy of individual rings in homocubanes in the same way as in the parent cyclobutane and cyclopentane.

Another interesting part of our work concerns the comparison of G3(MP2)B3LYP and MM results. Inspection of Table 1 indicates that in general, enthalpies and SE calculated by the two methods show parallel trends along the series of homocubanes. For example, G3 vs MM enthalpies have linear correlation coefficient of 0.997 and STD of 9.6. However, the problem with MM values is that they exhibit considerable discrepancies depending on the force field being used (see examples in Table 1). While the force field parametrizations are continuously being improved the problem of reliability remains. Furthermore, the discrepancy between experimental and MM enthalpy in the case of **7** is too large for MM results to be considered fully reliable (Table 1). It may be useful for diagnostic purposes to consider cases where G3-MM discrepancies are particularly large. Considering that the error in thermochemical measurements is of the order of 5 kJ/mol (Table 1) and that the typical reliability of G3(MP2)/B3LYP method is of the order of 3 kJ/mol, we shall consider G3-MM discrepancies as being significant only if they are > 10 kJ/mol. Such discrepancies are marked by an asterisk in Table 1. The largest G3-MM discrepancies occur in homocubanes which have rings of many different sizes (e.g. **12** and **14**). Our results also offer the possibility of direct comparison between G3 and MM methods on the basis of experimental results. For instance, future measurements of relative stability of **10** and **16** could be used as a direct check on reliability of G3 and MM values, because the two methods give opposing predictions for the relative stability of the two compounds (Table 1).

### CONCLUSION

In this work we have used high-level calculations to investigate enthalpies of formation and steric strain energies

for homocubanes. The calculations revealed that the number of four-member (cyclobutane) rings present in the molecule is the single largest factor influencing enthalpy and strain energy; the larger the number of such rings, the larger the strain energy (and enthalpy) becomes. We have demonstrated that it is feasible to perform high level thermochemical calculations for molecules the size of homocubanes using modest computational resources. The ab initio results are in better agreement with scarce experimental results and are more internally consistent than the MM results. Our recommendation therefore is to use ab initio methods when generating thermochemical databases in preference to MM methods.

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