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The Baeyer strain in small ring systems does not originate from a decrease in nucleus–electron attraction

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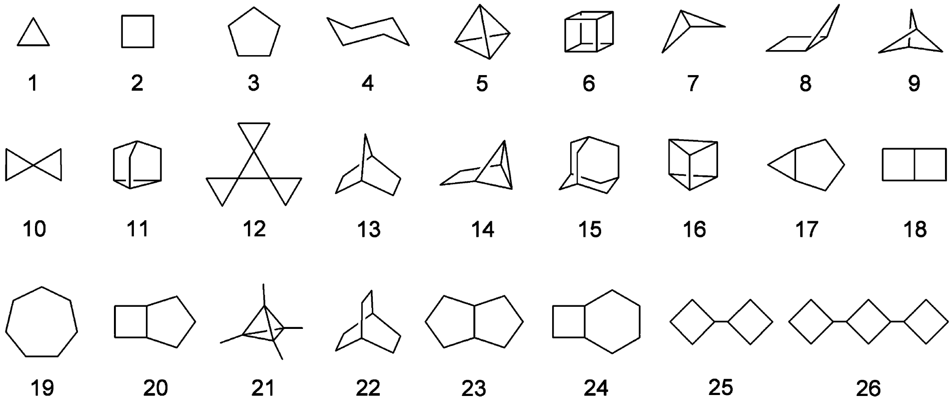
Abstract—Differences in nucleus–electron attraction compared to acyclic compounds are not related to ring or Baeyer strain. They result from interaction imbalances in the underlying reactions.

In a recent publication Barić and Maksić provided a theoretical analysis of ring or Baeyer strain in a series of molecules that ranged from cyclopropane to adamantane.[1] From the investigation of what they termed quasihomodesmotic reactions, they reached several conclusions concerning the Baeyer strain that, in spite of its fundamental importance in organic chemistry, it is not directly observable like other important concepts, for example, aromaticity.[2–4] The expression quasihomodesmotic was introduced to acknowledge that a C–C- or a C–H-bond in cyclopropane or cubane is not directly comparable with such bonds in propane or isobutane. However, it is just this difference that shows up in the reaction energy, which is directly related to the strain energy E_{st}. It was shown that basis sets like cc-pvtz are sufficient to treat this kind of molecules and that correlation effects are of minor importance due to a strong cancellation of static and dynamic correlation in these quasihomodesmotic reactions. From a Hartree–Fock energy component analysis in which the contribution of the potential energy ΔV to the strain energy E_{st} is subdivided into contributions from electron–electron repulsion ΔV_{ee}, nucleus–electron attraction ΔV_{ne} and nucleus–nucleus repulsion ΔV_{nn} the authors finally



Scheme 1. Molecules considered in this work.

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concluded that Baeyer strain in small ring systems originates from a decrease in nucleus–electron attraction compared to acyclic compounds.[1]

One could ask why the authors concentrate on ΔV_{ne} and not on ΔV_{ee} or ΔV_{nn}, which shows the same trends with opposite sign. However, this is primarily a semantic question that we do not want to follow. In this Letter we will demonstrate that the conclusion drawn in Ref. 1 on ΔV_{ne} does not hold. To do so, we use the same 15 saturated hydrocarbons as in Ref. 1 (molecules **1**–**15** in Scheme 1) together with 11 others (**16**–**26**). We also include a planar version of cyclohexane (**4pl**). With the abbreviations **E** for ethane, **P** for propane, **IB** for isobutane and **NP** for neopentane the corresponding quasi-homo-desmotic reactions read as follows:

R1 3**P** → **1** + 3**E**
R2 4**P** → **2** + 4**E**
R3 5**P** → **3** + 5**E**
R4 6**P** → **4** + 6**E**
R5 4**IB** → **5** + 6**E**
R6 8**IB** → **6** + 12**E**
R7 2**P** + 2**IB** → **7** + 5**E**
R8 3**P** + 2**IB** → **8** + 6**E**
R9 3**P** + 2**IB** → **9** + 6**E**
R10 4**P** + **NP** → **10** + 6**E**
R11 3**P** + 4**IB** → **11** + 9**E**
R12 6**P** + 3**NP** → **12** + 12**E**
R13 5**P** + 2**IB** → **13** + 8**E**
R14 2**P** + 4**IB** → **14** + 8**E**
R15 4**P** + 4**IB** → **15** + 12**E**
R16 6**IB** → **16** + 9**E**
R17 4**P** + 2**IB** → **17** + 7**E**
R18 4**P** + 2**IB** → **18** + 7**E**
R19 7**P** → **19** + 7**E**
R20 5**P** + 2**IB** → **20** + 8**E**
R21 4**NP** → **21** + 6**E**
R22 6**P** + 2**IB** → **22** + 9**E**
R23 6**P** + 2**IB** → **23** + 9**E**
R24 6**P** + 2**IB** → **24** + 9**E**
R25 6**P** + 2**IB** → **25** + 9**E**
R26 8**P** + 4**IB** → **26** + 14**E**

Writing the reactions in this order assures that reaction energies correspond directly to the positive defined strain energies.

Reaction energies ΔE were calculated as in Ref. 1. Each molecule was optimized at the HF-level implying a cc-pvtz basis. A subsequent frequency calculation yielded the zero point vibrational energy (ZPVE) and ensured that the optimized geometry is a minimum on the potential energy surface.[5] Correlation contributions to ΔE were estimated from MP2 calculations with the same basis set at the HF optimized geometries. All calculations were performed with GAUSSIAN 03.[6] To make certain that our procedure is the same as described in Ref. 1, we recalculated 9 of the originally 15 reactions and did not find any significant deviations from the results provided in this Letter.

At the HF level the strain energy E_{st} is directly given by ΔE_{HF}. A somewhat more advanced estimate is obtained from

$$E_{\mathrm{st}} = \Delta E_{\mathrm{HF}} + \Delta\mathrm{ZPVE} + \Delta\mathrm{MP2} \tag{1}$$

ΔE_{HF} and E_{st} are shown in Table 1 together with ΔZPVE, ΔMP2 and the potential energy components ΔV_{ne}, ΔV_{ee} and ΔV_{nn}. ΔT and ΔV are not shown because they are not independent quantities due to the validity of the virial theorem. The latter was enforced by appropriate scaling.[7] ΔZPVE is always negative and ΔMP2 always positive. This leads to a considerable cancellation between these two corrections, with the net effect that, in many cases, E_{st} is close to ΔE_{HF}. The rows in bold numbers contain data for four pairs and one quadruple of isomers. In these cases the differences between ΔV_{ne} correspond directly to the differences between the V_{ne} of the isomers because all other contributions to ΔV_{ne} are the same. An equivalent conclusion holds for ΔV_{ee} and ΔV_{nn}.

When we consider reactions 1–15, the reactions originally investigated in Ref. 1, it is indeed intriguing that the only two compounds for which ΔV_{ne} is negative are the nearly strain free molecules cyclohexane (**4**) and adamantane (**15**). This observation led Barić et al. to conclude that a positive contribution of ΔV_{ne} to the strain energy, which means a nucleus–electron attraction that is less favourable in the strained compound compared to open chain analogues, is the main source of Baeyer strain.

However, this ideal picture is immediately destroyed when we consider a cyclohexane, that is, forced to planarity (**4pl**). The strain energy rises from practically 0 to 29 kcal/mol, however, ΔV_{ne} stays negative. The moderately strained systems cycloheptane (**19**) and bicyclo[2,2,2]octane (**22**) also show a negative ΔV_{ne}. Compound **23** is more strained than cyclopentane (**3**) but ΔV_{ne} is negative in contrast to what is found for **3**. Compounds **20** and **24** exhibit nearly equal strain, which is somewhat larger than in cyclobutane (**2**) alone, but ΔV_{ne} is positive for **20** and negative for **24**. The most convincing proof that the sign of ΔV_{ne} is not related to the Baeyer strain results from a comparison of **2**, **25** and **26**. As expected, the strain rises nearly linearly with the number of four rings but ΔV_{ne} changes from largely positive over moderately positive to strongly negative. The comparison of the isomers also leads to intriguing results: ΔV_{ne} increases with increasing strain for isomers **4**/**4pl**, **13**/**20** and **22**/**23**/**24**/**25** but it decreases for pairs **8**/**9** and **17**/**18**. ΔV_{ee} and ΔV_{nn} show the same trends as ΔV_{ne} with opposite signs. It is obvious that none of the components of ΔV has anything to do with Baeyer strain.

To understand what causes the magnitude and the sign of the components of ΔV, we have to consider the interaction imbalance embedded in the underlying reactions.[8,9] The concept of interaction imbalance is most easily understood for ΔV_{nn} because of its classical nat-

Table 1. Calculated energies for reactions R1–R26

	ΔV_{ne}	ΔV_{ee}	ΔV_{nn}	ΔE_{HF}	ΔZPVE	ΔMP2	E_{st}
R1	56522	−28298	−28172	26.6	−3.2	3.4	26.8
R2	42641	−21299	−21290	26.0	−2.8	2.5	25.7
R3	17166	−8560	−8592	6.6	−2.1	1.3	5.8
R4	**−17888**	**8953**	**8937**	**0.9**	**−1.4**	**0.5**	**0.0**
R4pl	**−9323**	**4747**	**4635**	**29.2**	**−1.3**	**1.6**	**29.5**
R5	224489	−112319	−111904	133.8	−12.2	12.5	133.5
R6	*252123*	*−125899*	*−125916*	*153.8*	*−14.0*	*19.2*	*159.0*
R7	133580	−66892	−66558	64.6	−6.7	6.9	64.8
R8	***109116***	***−54583***	***−54427***	***53.2***	***−5.5***	***6.7***	***54.5***
R9	***104871***	***−52473***	***−52264***	***67.1***	***−4.9***	***2.1***	***64.3***
R10	130897	−65514	−65276	57.8	−6.6	10.6	61.8
R11	*113323*	*−56690*	*−56563*	*34.7*	*−6.8*	*7.2*	*35.1*
R12	186633	−93438	−92954	120.2	−13.7	22.7	129.2
R14	*167063*	*−83587*	*−83343*	*66.3*	*−8.3*	*10.3*	*68.3*
R15	*−89701*	*44885*	*44823*	*3.8*	*−4.4*	*1.2*	*0.6*
R16	259008	−129508	−129222	138.5	−13.3	16.0	141.2
R17	**75676**	**−37851**	**−37759**	**32.8**	**−5.2**	**5.9**	**33.5**
R18	**75167**	**−37516**	**−37546**	**52.6**	**−5.8**	**6.5**	**53.3**
R19	−58937	29501	29454	8.9	−1.3	1.2	8.8
R13	**19389**	**−9668**	**−9691**	**15.0**	**−3.8**	**1.2**	**12.4**
R20	**31112**	**−15499**	**−15550**	**31.3**	**−4.9**	**4.3**	**30.7**
R21	223224	−111614	−111371	119.6	−10.6	23.0	132.0
R22	**−36363**	**18225**	**18234**	**11.0**	**−3.4**	**0.9**	**8.5**
R23	**−20426**	**10262**	**10186**	**11.0**	**−4.0**	**2.7**	**9.7**
R24	**−17747**	**8902**	**8911**	**33.3**	**−4.3**	**1.5**	**30.5**
R25	**2586**	**−1238**	**−1248**	**49.4**	**−6.0**	**5.0**	**48.4**
R26	−122448	61317	61278	73.0	−9.3	7.3	71.0

All values in kcal/mol. ΔE_{HF}: reaction energy at the HF-level. ΔV_{ne}, ΔV_{ee} and ΔV_{nn}: components of the potential energy contribution $\Delta V = 2\Delta E_{\mathrm{HF}}$. ΔZPVE: zero vibrational energy contribution. ΔMP2: correlation contribution as estimated at the MP2-level. E_{st}: strain energy according to Eq. 1. Data in italics are from Ref. 1. Data of isomers are in bold and bold italics.

ure. For a hydrocarbon molecule V_{nn} can be expressed as

$$V_{\mathrm{nn}} = \sum_{A,B} \frac{Z_A Z_B}{R_{AB}} = 36 \sum_{A<B} \frac{1}{R_{C_A C_B}} + 6 \sum_{A,B} \frac{1}{R_{C_A H_B}} + \sum_{A<B} \frac{1}{R_{H_A H_B}} \qquad (2)$$

If other atoms are present besides C and H the above formula has to be expanded accordingly. Counting the number of CC-, CH- and HH-interactions on both sides of the reaction equation leads to what is shown in Table 2. For R1, for example, there are 6 CC-, 54 CH- and 60 HH-interactions on the right side compared to 9 CC-, 72 CH- and 84 HH-interactions on the left side. The number of interactions differs considerably between the two sides. We call a reaction such as R1 in which the number of interactions on the left side is larger than on the right side left side unbalanced.

The consequences of such an imbalance become obvious when the individual contributions to ΔV_{nn} are arranged in such a way that interactions, which are similar on both sides of the reaction equation, are grouped together. This yields what we call balanced terms. As the number of interactions is not the same on both sides, some of the contributions cannot be grouped and result in unbalanced terms. In Table 3 this is exemplified for R1. Columns three and four show internucleus distances that appear on the left (R_{l}) and on the right (R_{r}) side of the reaction equation. The numbers in column 2 tell us how often a certain pair or an unmatched distance appears. Unmatched distances appear only on the left side because all three types of interactions (CC, CH and HH) are left side unbalanced (see Table 2). Column

Table 2. Number of nucleus–nucleus interactions on the left and the right sides of the reaction equation separated by a slash

	CC	CH	HH	Total	IMB
R1	9/6	72/54	84/60	165/120	240
R2	12/10	96/80	112/88	220/178	192
R3	15/15	124/110	140/120	275/245	104
R4	18/21	148/144	156/168	330/321	−72
R5	24/12	160/88	180/96	364/196	948
R6	48/40	320/208	360/208	728/456	1112
R7	18/11	128/84	146/90	292/184	572
R8, R9	21/16	152/112	174/118	347/246	476
R10	22/16	156/112	178/118	356/246	540
R11	33/30	232/118	264/180	529/388	516
R12	48/48	324/252	366/246	738/556	552
R13, R20	27/29	200/180	230/186	457/395	92
R14	30/23	208/144	236/148	474/315	724
R15	42/57	308/304	348/300	694/661	−516
R16	36/24	240/144	270/150	546/318	1126
R17, R18	24/22	176/144	202/150	402/316	316
R19	21/28	168/182	196/196	385/406	−336
R21	40/34	240/168	265/156	544/358	834
R22, R23, R24, R25	30/37	224/220	258/226	512/483	−196
R26	48/80	352/408	404/400	804/888	−1484

IMB: imbalance index according to Eq. 3.

Table 3. Balanced and unbalanced contributions to ΔV_n for reaction R1

Interaction	N	R_l (Å)	R_r (Å)	Balanced terms (kcal/mol)	Unbalanced terms (kcal/mol)
CC	3	1.524964	1.495875	457.3	
	3	1.524964	1.523873	16.8	
	3	2.542521			−14105.1
ΣCC				474.2	−14105.1
CH	6	1.084137	1.073251	111.8	
	12	1.085137	1.083949	24.1	
	6	1.085852	1.083949	19.3	
	12	2.166359	2.213555	−235.3	
	6	2.169163	2.166560	6.6	
	12	2.145246	2.166560	−109.6	
	12	2.805124			−8523.1
	6	3.485604			−3429.6
ΣCH				−183.0	−11952.7
HH	3	1.737354	1.802300	−20.7	
	6	1.751587	1.749914	1.1	
	12	1.752396	1.749914	3.2	
	6	2.483806	2.505508	−6.9	
	6	2.483806	2.520577	−11.7	
	12	2.506184	2.520577	−9.1	
	6	2.631717	3.086398	−111.5	
	9	3.053536	3.068495	−4.8	
	3	3.053536			−326.2
	6	3.161329			−630.2
	12	3.798680			−1049.0
	3	4.316222			−230.8
ΣHH				−160.4	−2236.2
Σ				130.8	−28294.0

See text for details.

5 shows the contributions to ΔV_{nn} (in kcal/mol) that result from 120 balanced terms. All these terms contribute only 131 kcal/mol, which is more or less negligible compared to the magnitude of ΔV_{nn}. Column 6 finally shows the contributions that result from the 45 unbalanced nucleus–nucleus interactions. They add up to −28294 kcal/mol, which is more than 99% of ΔV_{nn}.[10]

From the example it is obvious that ΔV_{nn} is completely dominated by unbalanced nucleus–nucleus interactions. If a reaction is left side unbalanced with a surplus of n,n-interactions on the educt side, ΔV_{nn} is negative because the contributions from the unbalanced terms enter with a negative sign. Most reactions considered in this study belong to that type. If the reaction is right side unbalanced it is just the opposite and ΔV_{nn} will become positive. Examples for reactions with an overall right side imbalance are R19 and R26, but for the latter the HH-interactions are still slightly left side unbalanced.

Table 1 shows that ΔV_{nn}, ΔV_{ee}, and $-\Delta V_{ne}/2$ behave in very similar ways. This parallelism is quite understandable because most of the electron density is concentrated around the nuclei. If the nucleus–nucleus repulsions are unbalanced a similar imbalance exists for the electron–electron repulsions and the nucleus–electron attractions. All three components of ΔV are prone to similar imbalances.

It should be mentioned at that point that for any saturated ring larger than seven the HH-interactions become right side unbalanced in addition to the CC- and CH-interactions that are already that way in cycloheptane (compare R19). This leads to a positive ΔV_{nn} irrespective of the geometry of the ring, unstrained, strained, or forced to planarity. Because of the previously noted parallelism between ΔV_{nn} and ΔV_{ne} such a positive ΔV_{nn} corresponds to a negative ΔV_{ne} for any saturated ring larger than six, strained or not.

Several of the investigated reactions are not adequately described by the overall imbalance shown in the second last column of Table 2 because the imbalance is different for different types of interactions. The overall imbalance of reactions 4, 13, 15, 20 and 22 to 25 is still on the left side but the imbalance of CC-interactions is on the right side. In such a case, the sign of ΔV_{nn} depends on the relative strength of the different imbalances. For R4, R15, R22, R23 and R24 the right side imbalanced CC-interactions outweigh a larger number of left side imbalanced CH- and HH-interactions and make ΔV_{nn} positive. However, in the case of R13, R20 and R25 the right side imbalance of CC-interactions is not strong enough to outweigh a left side imbalance of CH- and HH-interactions and therefore ΔV_{nn} stays negative. To deal with these mixed cases we introduce a very simple imbalance index IMB

$$\mathrm{IMB} = 36\Delta\mathrm{CC} + 6\Delta\mathrm{CH} + \Delta\mathrm{HH} \qquad (3)$$

ΔCC, ΔCH and ΔHH are the differences of the respective interactions on the right and left sides of the reaction equation. They are positive for left side imbalance and negative for right side imbalance. The IMBs for all considered reactions are provided in the last column of Table 2. A plot of ΔV_{ne} against IMB is shown in the graphical abstract. Plots of $-2\Delta V_{ee}$ or $-2\Delta V_{nn}$ against IMB would be indistinguishable on the given scale. IMB is positive in all cases where ΔV_{nn} is negative and negative in all cases where ΔV_{nn} is positive except R25. As simple as IMB is defined the correlation with the components of ΔV is quite strong. The sign and the magnitude of all three components are primarily determined by the interaction imbalances that are characteristic for the underlying reaction and have nothing to do with Baeyer strain or any other quantity the reaction energy may be associated with.

The previously discussed irregularities in the connection between ΔV_{ne} and E_{st} that appear for different groups of isomers are also easy to understand. However, the key is ΔV_{nn} and not ΔV_{ne}. In planar cyclohexane, for example, the average internuclear distance is larger than for the relaxed geometry. This reduces the nucleus–nucleus repulsion in **4pl** compared to **4**. As both molecules appear on the right side of the reaction equation $\Delta V_{nn} = \Sigma V_{nn}(\text{product}) - \Sigma V_{nn}(\text{educt})$ decreases when we exchange **4** by **4pl**. As ΔV_{ne} is close to $-2\Delta V_{nn}$ the reduced compactness of **4pl** explains the observed increase of ΔV_{ne}, which in this case parallels an increase in strain. A similar situation occurs in the isomer pair **13**/**20** and in series **22**–**25**: the molecules become less compact, which leads to a decrease of ΔV_{nn} and an increase of ΔV_{ne}, but the strain increases due to the appearance of smaller rings. The opposite behaviour is observed for pairs **8**/**9** and **17**/**18**: in these cases, the compactness increases with increasing strain and ΔV_{nn} and ΔV_{ee} rise, which in turn causes ΔV_{ne} to decrease.

Even within groups of isomers there is no correlation between changes in nucleus–nucleus repulsion or nucleus–electron attraction and strain. The individual components of the potential energy contribution ΔV are almost exclusively determined by the interaction imbalance of the underlying reaction. Only if added together the imbalances in the attractive and repulsive components cancel each other so that ΔV becomes twice the reaction energy. The individual components themselves have no physical meaning and their discussion does not reveal information that relates to an individual molecule.

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