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Strain Release is Not Enough.

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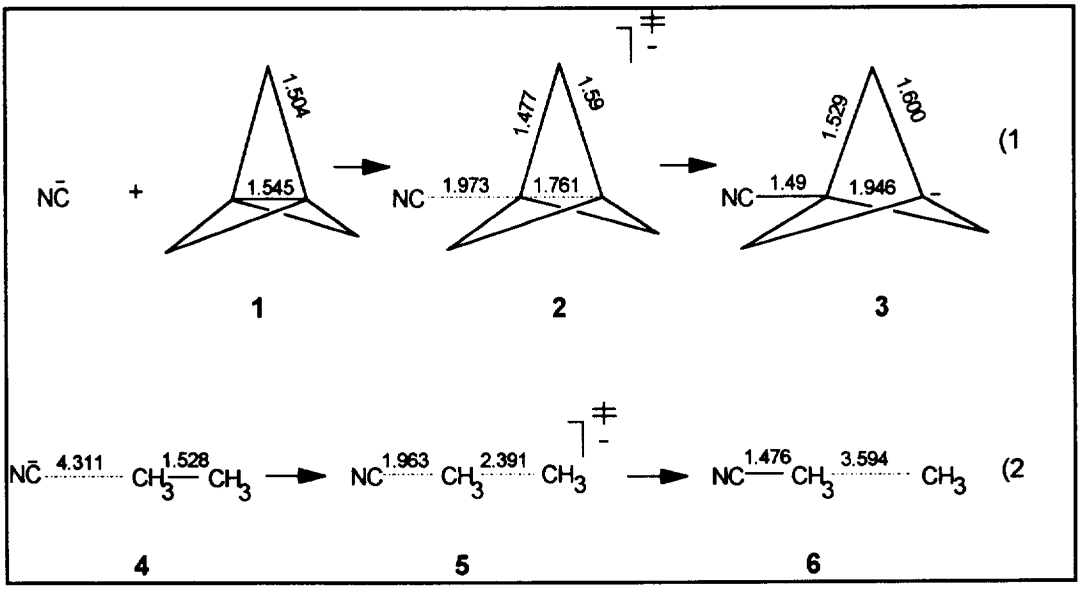
***Abstract*:**The activation barrier for the nucleophilic attack of CN^- on [1.1.1]-propellane is lowered by 60.7 kcal (compared to the strain free analog) while the total strain energy released in the reaction is only 45 kcal showing that strained molecules react faster not only because of partial strain release at the transition state.

Strained compounds are notorious for exhibiting reaction rates which drastically exceed those of their unstrained analogs. This effect is usually interpreted in terms of a "cause and effect" argument; namely, that the activation energy is lowered due to partial strain relief at the transition state.[1] Yet, it should always be kept in mind that the existence of a correlation between two parameters does not necessarily imply a "cause and effect" relationship between them. In a recent publication we have shown[2] that both, rate enhancement and strain, seem to stem from a higher primary cause - *molecular deformation*. Thus, deforming bond lengths and bond angles induces (a) a rise in the energy content, i.e., strain and (b) orbital rehybridization. Of these two it is mainly the latter which is responsible for rate enhancement and not "partial strain relief at the transition state". Orbital rehybridization results in the frontier orbitals becoming more amenable for bonding. The transition state is, therefore, reached earlier along the reaction coordinate and hence, the reaction barrier is lowered.

If the above argument is correct, then in principle, one should be able to find a case where the reduction of the barrier height due to the frontier orbital effect is bigger than the total strain energy released in the reaction. Such a case will unambiguously prove that other factors beside strain relief at the transition state are responsible for rate enhancement, and that orbital rehybridization effects are not synonymous with partial strain relief at the transition state. To be a suitable substrate for this purpose the molecule must be highly distorted. A suitable reaction would be one in which the "distorted" orbitals are involved in the bonding process. The third condition to be met is that not much strain energy be released in this reaction. [1.1.1]-propellane (**1**) was found to be an optimum choice. According to a majority of the studies[3], the central bond of **1** deviates markedly from the normal sp^3 hybridization and **1** is also known to undergo nucleophilic attacks which cleave the central bond.[4] The strain energy of [1.1.1]-propellane is 98 kcal/mol[1b] and the strain energy of the parent compound of the product, 1,1,1-bicyclopentane, is 68 kcal/mol.[1b] Therefore, a total strain energy of 30 kcal/mol is expected to be released in the reaction. The reaction shown in equation 1 (Scheme 1) was computationally studied and that in equation 2 was used as its reference - strain free- analog.



Scheme 1.

The computations were performed using the Gaussian 92 program and all structure optimizations were performed at the RHF/6-31+G* level.[5] The transition states of both reactions were characterized by frequency analysis. Major geometrical parameters are given in scheme 1. Energies at the RHF/6-31+G* and the MP4/6-31+G*//6-31+G* levels are given in Table 1.[6]

Table 1: Energies (in au.) of the species in Scheme 1.

	CN^-	**1**	**2**	**3**
6-31+G*	-92.3148718	-192.6963900	-284.9709771	-284.9928191
MP4/6-31+G* //6-31+G*	-92.6213489	-193.4196985	-286.0189653	-286.0304429

	4	**5**	**6**
6-31+G*	-171.5449187	-171.4078674	-171.4547565
MP4/6-31+G* //6-31+G*	-172.1582153	-172.0365119	-172.0740787

In a normal SN2 reaction the reactants are located at the bottom of a potential well in a form of an ion - dipole complex. In the present case no such complex was found for the reaction of **1** with CN^-. The repulsion between these two species results from the absence of a dipole in the ground state of **1**, the negative charge on the bridgehead carbon and the absence of a compensating attractive interaction such as the one present between the CN^- and the three hydrogen atoms of the methyl group in reaction 2. In both reactions the nucleophile's approach was restricted to the line of the cleaved C-C bond.

At the RHF/6-31+G* level the reaction and activation energies of the first reaction are 11.6 and 25.3 kcal and for the second reaction 56.6 and 86 kcal, respectively. Using the traditional approach, the difference in the reaction energies corresponds to the strain energy released in reaction 1 (45 kcal) and the difference in the activation energies corresponds to the amount of strain energy released at the transition state (60.7 kcal). The fact that by this approach more strain energy is released at the transition state (135% at the RHF/6-31+G* and 136% at the MP4/6-31+G*//6-31+G* levels) than the total amount released in the overall reaction shows clearly that attributing rate enhancement to strain alone is wrong.

Examination of the geometrical data in scheme 1 shows that the transition state for the nucleophilic attack on **1** is located, roughly, half way between reactants and products. Assuming, in the best tradition of the Linear Free Energy Relationship approach[7], that strain energy release propagates linearly with the geometrical parameters, at the transition state of the reaction of **1** only 50% of the total reaction strain energy should be released. Therefore, even according to the traditional approach, the major part (ca. two thirds) of the rate enhancement in the reaction of this highly strained molecule cannot be attributed to strain energy release at the transition state. Enhanced incipient bonding between the HOMO of the nucleophile and the LUMO of **1** is likely to be the major contributor to the lower activation energy.

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