Substituent Steric Strain: Enthalpic Estimates for the Consequences of Interactions between Bulky Substituents

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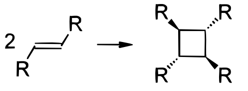
Introduction

It is well established that steric hindrance imposed by the size of substituents modifies the chemical reactivity of molecules with respect to derivatives bearing smaller substituents.[1,2] The relative stability of structural alternatives or bonding arrangements is also dependent upon the steric presence of the substituents. Examples of sterically enforced structural novelty include an isolable Dewar benzene[3] and a linear ketenimine.[4] However, most significant has been the widespread development of structurally novel inorganic compounds containing multiple bonds and/or low-coordinate environments for the heavier elements of groups 13,[5] 14,[6,7] and 15,[8] which has been made possible by the stabilizing influence of bulky substituents.[9]

From a kinetic perspective,[10,11] the steric shield provided by bulky substituents is envisaged as hindering the approach of molecules and preventing oligomerization and other types of reactions. The thermodynamic consequences of steric hindrance have been categorized for many functional groups;[1] however, the steric strain associated with the presence of large bulky substituents has only been alluded to.[12] The comprehensive and systematic treatment already given to bond angle distortion or ring strain[13] is more difficult for substituent steric interactions, as they are a function of substituent size and shape as well as proximity and relative orientation. Moreover, theoretical analysis of realistic systems involves large molecules, so that high-level calculations are impractical.

In an attempt to assess the magnitude of substituent steric strain, we have determined enthalpies of cyclodimerization (cyclobutane) for a series of *trans*-1,2-substituted alkenes (eq 1) possessing substituents of varying sizes using molecular mechanics and semiempirical calculations. This well-defined model system provides results which clearly demonstrate the influence of substituent type (size) on the relative thermodynamic stability of the ethene with respect to the corresponding cyclobutane. In addition, similar calculations for carbenes and disilenes illustrate the general implications for the conclusions.



(1)

Computational Methods

Geometry optimizations were performed with two molecular mechanics packages, PCMODEL[14] and MM3 (94),[15] as well as the semiempirical method AM1,[16] from the Gaussian packages of programs. Dimerization enthapies for ethene derivatives were determined for fully optimized structures, although the dimers were restricted to a cyclic (cyclobutanes) *trans*,*trans* stereochemistry to minimize the geometric

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Table 1. Calculated Enthalpies of Cyclodimerization for 1,2-Substituted (R) Alkenes (kJ/mol)

R	PCModel[a]	MM3[a]	AM1[b]
H	−87	−85	−142
Me	−84	−83	−77
^{t}Bu	−10	−7	−23
Ph	−65	+19	−47
Mes	+21	+68	+46
Trip	+164	+282	+173
Mes*	+429	+395	+475

[a] Heat of formation of cyclobutane: 2(heat of formation of alkene). [b] Total energy of cyclobutane: 2(total energy of alkene).

Table 2. Calculated (PCModel) Absolute Strain Energies (kJ/mol) for 1,2-Substituted Alkenes and 1,2,3,4-Substituted (R) Cyclobutanes

R	ethene	cyclobutane	R	ethene	cyclobutane
H	0	110	Mes	150	360
Me	0	100	Trip	220	740
^{t}Bu	50	190	Mes*	330	1200
Ph	100	290			

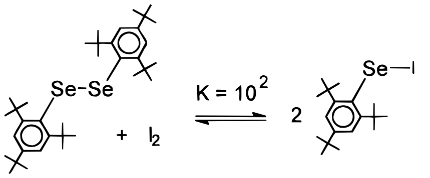
and conformational options. Rotational, vibrational, and translational energies with temperature corrections had a negligible effect on the values.

Results and Discussion

The enthalpies of alkene dimerization (eq 1) have been determined from calculated (geometry optimized) heats of formation (PCMODEL and MM3) and absolute energies (AM1) for a series of 1,2-disubstituted (R) alkenes and their corresponding 1,2,3,4-tetrasubstituted cyclobutanes [R = methyl (Me), *tert*butyl (^{t}Bu), phenyl (Ph), mesityl (Mes), 2,4,6-triisopropylphenyl (Trip), 2,4,6-tri-*tert*butylphenyl (Mes*)]. The three computational methods reveal reasonable trends with similar orders of magnitude for the enthalpic estimates (Table 1). Consistent with previous reports,[13] the dimerization of ethene to cyclobutane is exoenthalpic, but as two hydrogen atoms are replaced by larger substituents, the dimerization energy becomes less exothermic and is slightly endothermic with mesityl substitution [R = $C_6H_2Me_3$ (Mes)]. The endothermicity of the reaction is significantly greater with R = $C_6H_2{}^iPr_3$ (Trip) and is more than doubled when R = $C_6H_2{}^tBu_3$ (Mes*). We attribute these trends to the imposition of substituent steric strain, calculated values for which are presented in Table 2.

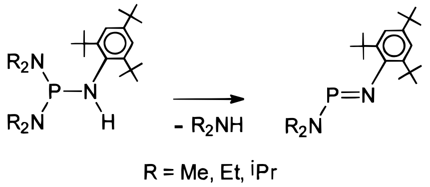
As expected, the calculated dimerization enthalpy for tetrasubstituted alkenes such as $Mes_2C{=}CMes($$_2$ (+2191 kJ/mol by PCModel; +1873 kJ/mol by MM3) is dramatically more endothermic than that for the corresponding 1,2-disubstituted alkene [Mes(H)C=C(H)Mes(+21 kJ/mol by PCModel; +68 kJ/mol by MM3)]. We have also calculated a substantially endothermic dimerization energy for the supermesityl-substituted carbene $Mes^*{}_2C$: (+458 kJ/mol by AM1).

Direct experimental evidence for the thermodynamic influence of substituents such as Mes* is available for systems involving atoms larger than carbon despite the longer bonds and consequential relatively lower substituent steric strain in these systems. For example, the equilibrium constant for eq 2



(2)

favors the iodoselenide Mes*SeI,[17] contrary to the recognized instability of Se−I covalent bonds with respect to the corresponding homoatomic bonds.[18] Observation of spontaneous elimination of amines from Mes*-substituted triaminophosphines to give iminophosphines (eq 3)[19] is likewise contrary to addition



(3)

reactions observed for ^{t}BuN=PR (R = ^{t}Bu or $SiMe_3$) with primary or secondary amines.[20] In this context, we recently described some comparative experimental data for phosphines, arsines, stibines, and bismuthines which offer some guidelines for the steric limits of the Mes* substituent.[21] The closest analogy to the calculated values presented here is provided by the dimerization process of the carbene-analogous diarylstannylenes (R_2Sn:), the first derivative of which was observed to be a dimeric distannene in the solid state[11] and a monomeric species in the gas phase.[22,23] More recently, dimerization and oligomerization of stannylenes were shown to be very sensitive to the type of substituent, with $Mes^*{}_2Sn$ monomeric in the solid state[7] and derivatives with slightly smaller substituents (Trip,[24] 2-*tert*butyl-4,5,6-trimethylphenyl[25]) forming solution-dissociable distannenes.

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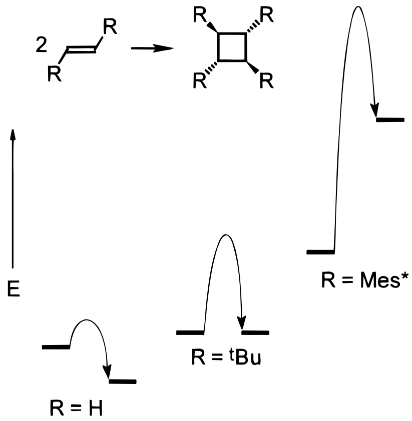

Figure 1. Qualitative energetic comparison for the cyclodimerization of ethene and ethenes 1,2-substituted by ᵗBu and Mes*.

The isolation and implied stability of compounds containing multiple bonds between heavier non-metal elements, such as silicon in $Mes_2Si{=}SiMes_2$,[26] do not allow for such direct conclusions, as their stability with respect to alternative structural arrangements may be solely due to the kinetic barrier imposed by the steric shield. Nevertheless, application of our computational approach to the disilene $Mes_2Si{=}SiMes_2$ provides a dimerization energy of +487 kJ/mol (MM3), which represents the thermodynamic component for the relative stability of the disilene with respect to the cyclotetrasilane $(Mes_2Si)_4$. As expected, the preference for the disilene $Mes_2Si{=}SiMes_2$ is less than that calculated for the corresponding alkene [$Mes_2C{=}CMes_2$ (+1873 kJ/mol by MM3)] but demonstrates a substantial substituent steric strain in the cyclosilane. There is no doubt that the effect of bulky substituents on the kinetic component of the dimerization process is also substantial.

In conclusion, enthalpic estimates of substituent steric strain confirm that the presence of bulky substituents such as Mes* renders ethenes thermodynamically stable with respect to their cyclobutane dimers, in addition to the enhancement of kinetic barriers to dimerization or other reactivity. The magnitude of the strain imposed by such substituents is so large that these conclusions apply to compounds containing heavier elements (albeit to a lesser degree), in spite of longer bonds, and allow for a better understanding of the chemistry of compounds containing multiply bonded and/or low-coordinate environments for the main group elements. Figure 1 provides a general qualitative guide for the significance of substituent steric interactions in the cyclodimerization of multiply bonded units.

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