ORGANIC LETTERS
2010
Vol. 12, No. 6
1320−1323

Why Are Some $(CH)_4X_6$ and $(CH_2)_6X_4$ Polyheteroadamantanes So Stable?

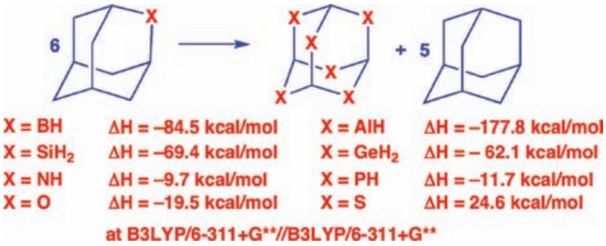
Yan Wang,[†,‡] Judy I-Chia Wu,[‡] Qianshu Li,[*,†] and Paul von Ragué Schleyer[*,‡]

School of Science, Beijing Institute of Technology, Beijing 100081, China, and
Department of Chemistry, Center for Computational Chemistry, University of Georgia,
Athens, Georgia 30602

qsli@bit.edu.cn; schleyer@chem.uga.edu

Received January 28, 2010

ABSTRACT



The representative isodesmic reactions shown in the Abstract graphic for $(CH)_4X_6$ hexaheteroadamantane derivatives reveal energetic nonadditivity to remarkably different extents: while the electropositive element stabilizations are exceptionally large and the pnictide and hexaoxaadamantane stabilizations are more modest, the sulfur and selenium analogues are destabilized. Similar behavior is exhibited by $(CH_2)_6X_4$ tetraheteroadamantanes. Analysis shows that aromaticity is not involved; the sign and magnitude of the nonadditivity depends on the interplay of hyperconjugation, electrostatic, and steric (lone pair repulsion) effects.

The principle of "additivity", that functional groups and other structural entities largely retain their character and properties upon being transferred from one "strain-free" molecular environment to another, greatly simplifies the interpretation and the study of chemistry.[1a−h] But understanding exceptions to "regular" behavior increases knowledge. Thus, energy differences between cyclically conjugated and linear polyenes depending on the number of π electrons are attributed to "aromaticity" and to "antiaromaticity."[2a,b] Large deviations from energetic additivity in aliphatic systems are also known[3a−d] but are far less well appreciated, investigated, and understood.

This paper is concerned with heteroadamantane derivatives, which despite having nonaromatic magnetic properties and normal geometrical parameters, exhibit remarkable energetic nonadditivity, in some cases far exceeding the aromatic stabilization of benzene.

Like adamantane itself, which is synthesized easily by exothermic isomerization of strained precursors,[4a,b] several of its polyhetero analogues were prepared by routes suggesting the advantages of having diamondoid over alternative skeletons. As early as 1860, Butlerow obtained urotropin (**14**) by the simple reaction of ammonia with formaldehyde.[5a] Its

---

[†] Beijing Institute of Technology.

[‡] University of Georgia.

(1) (a) Benson, S. W.; Buss, J. H. *J. Chem. Phys.* **1958**, *29*, 546. (b) Benson, S. W. *Thermochemical Kinetics*; Wiley-Interscience: New York, 1976. (c) Cohen, N.; Benson, S. W. *Chem. Rev.* **1993**, *93*, 2419. (d) Wodrich, M. D.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 2135. (e) Hayes, M. Y.; Li, B. Q.; Rabitz, H. *J. Phys. Chem. A* **2006**, *110*, 264. (f) Roganov, G. N.; Pisarev, P. N.; Emel'yanenko, V. N.; Verevkin, S. P. *J. Chem. Eng. Data* **2005**, *50*, 1114. (g) Yu, J.; Sumathi, R.; Green, W. H., Jr. *J. Am. Chem. Soc.* **2004**, *126*, 12685. (h) Saraf, S. R.; Rogers, W. J.; Mannan, M. S.; Hall, M. B.; Thomson, L. M. *J. Phys. Chem. A* **2003**, *107*, 1077.

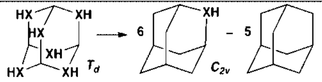
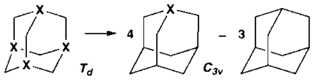
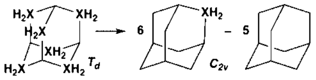
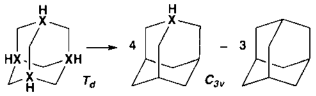
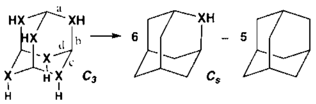
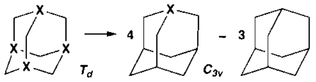
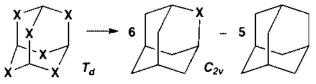
(2) See, e.g. :(a) Schleyer, P. v. R. *Chem. Rev.* **2001**, *101*, 1115–1118. (b) Schleyer, P. v. R. *Chem. Rev.* **2005**, *105*, 3433–3435.

(3) See, e.g.: (a) Dill, J. D.; Schleyer, P. v. R.; Pople, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 1663–1668. (b) Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6393–6394. (c) Salzner, U.; Schleyer, P. v. R. *Chem. Phys. Lett.* **1992**, *190*, 401–406. (d) Salzner, U.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1993**, *115*, 10231–10236. (e) Wiberg, K. B.; Rablen, P. R. *J. Am. Chem. Soc.* **1993**, *115*, 614–625.

(4) (a) Schleyer, P. v. R. *J. Am. Chem. Soc.* **1957**, *79*, 3292. (b) Schleyer, P. v. R.; Williams, J. E., Jr.; Blanchard, K. R. *J. Am. Chem. Soc.* **1970**, *92*, 2377–2386.

10.1021/ol1002187

Table 1. Nonadditivity of Poly-heteroadamantanes $(CH)_4(XH)_6$ and $(CH_2)_6X_4$ (X = B, Al, Ga, N, P, As), $(CH)_4(XH_2)_6$ and $(CH_2)_6(XH)_4$ (X = Si, Ge), and $(CH)_4X_6$ (X = O, S, Se) (Δ*H*, in kcal/mol at B3LYP/6-311+G** + ZPE) Evaluated by Isodesmic Reactions Shown below[a]

isodesmic reactions	X	ΔH	C–X	$q_{(C)}$	$q_{(X)}$	NICS(0)
	**1, B**	84.46	1.571	−1.24	0.71	5.95
	2, Al	177.75	1.954	−2.00	1.49	2.19
	3, Ga	148.25	1.983	−1.76	1.26	2.01
	**4, B**	34.63	1.591	−1.14	0.98	−5.07
	5, Al	111.37	1.978	−1.62	1.68	6.89
	6, Ga	101.60	2.008	−1.43	1.44	11.95
	**7, Si**	69.43	1.898	−1.62	1.20	−0.50
	8, Ge	62.05	1.985	−1.46	1.03	−0.15
	**9, Si**	45.90	1.895	−1.35	1.43	−0.50
	10, Ge	43.99	1.981	−1.22	1.25	0.33
	**11, N**	9.72	a-b-c-d:1.470-1.463-1.474-1.483	0.32	−0.70(±0.02)	4.59
	12, P	11.65	1.885-1.891-1.885-1.879	−1.18	0.65	3.01
	13, As	18.78	2.007-2.014-2.007-2.000	−1.23	0.71(±0.01)	3.09
	**14, N**	11.31	1.477	0.00	−0.58	8.34
	15, P	2.47	1.871	−1.05	0.85	6.15
	16, As	5.29	1.993	−1.07	0.92	4.03
	**17, O**	19.53	1.412	0.67	−0.58	5.62
	18, S	−24.59	1.840	−0.71	0.30	4.42
	19, Se	−18.04	1.983	−0.90	0.43	5.43

[a] CX bond lengths in Å, NBO charges (B3LYP/6-311+G**), and NICS (PW91/6-311+G**) at cage centers (NICS(0), in ppm) are also given. The B3LYP/6-311+G**-optimized geometries were used throughout.

C_6N_4 tetraazaadamantane structure was determined definitively by X-ray analysis in 1922.[5b] Molecules with the C_4B_6 hexaboraadamantane skeleton form by pyrolysis, e.g., BMe_3 gave $(CH)_4(MeB)_6$ ca. 25% yield,[6a,b] and dimerization of a C_2B_3-closo-carbaborane gave $(CMe)_4(EtB)_6$.[6c] Fort's generalization, "Almost all of the elements in groups 13, 15, and 16 can be incorporated into an adamantane skeleton",[7] has been amply extended in the ensuing three decades.[8] Indeed, hexabora- (**1**, see Table 1),[6a−e] hexagalla- (**3**),[9] tetraaza- (**14**),[5a−d] hexathia- (**18**),[10a−f] and hexaselenaadamantane (**19**)[11] representatives have been synthesized and characterized experimentally. Hexagallaadamantane (**3**), $(GaR)_6(CR')_4$, derivatives were synthesized by treating alkynes (R′C≡CH; R′ = Me, *n*-Pr) with dialkylgallium hydrides (R_2GaH; R = Me, Et).[9] Most recently, arsinicin A, a tetraarsenaadamantane derivative, was isolated from a sponge in the southwest Pacific Ocean.[12]

Nevertheless, no special thermochemical stability was associated with adamantane[4a,b] or with other diamondoid

---

(5) (a) Butlerow, A. *Ann.* **1860**, *115*, 322–327. (b) Dickinson, R. G.; Raymond, A. L. *J. Am. Chem. Soc.* **1923**, *45*, 22–29. (c) Mak, T. C. W.; Li, W. K.; Yip, W. H. *Acta Crystallogr.* **1983**, *C39*, 134–136. (d) Chou, M.; Lessinger, L. *Acta Crystallogr.* **1987**, *C43*, 322–324.

(6) (a) Brown, M. P.; Holliday, A. K.; Way, G. M. *J. Chem. Soc., Dalton Trans.* **1975**, *2*, 148–151. (b) Brown, M. P.; Holliday, A. K.; Way, G. M.; Whittle, R. B.; Woodard, C. M. *J. Chem. Soc., Dalton Trans.* **1977**, 1862–1866. (c) Köster, R.; Seidel, G.; Wrackmeyer, B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 326–328. (d) Rayment, I.; Shearer, H. M. M. *J. Chem. Soc., Dalton Trans.* **1977**, *13*, 6–138. (e) Wrackmeyer, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 7731–7732.

(7) Fort, R. C., Jr. *Adamantane—The Chemistry of Diamond Molecules*; Marcel Dekker: New York, 1976; pp 106−115.

(8) Vittal, J. J. *Polyhedron* **1996**, *15*, 1585–1642.

(9) Uhl, W.; Cuypers, L.; Neumuller, B.; Weller, F. *Organometallics* **2002**, *21*, 2365–2368.

(10) (a) Stetter, H. *Angew. Chem.* **1954**, *66*, 217. (b) Olsson, K. *Acta Chem. Scand.* **1958**, *12*, 366. *Ark. Kemi.* **1959**, *14*, 371. (c) Pickardt, J.; Rautenberg, N. *Z. Naturforsch.* **1986**, *41b*, 409. (d) Fredga, A.; Bauer, H. *Ark. Kern.* **1950**, *2*, 113–118(Et) (e) Aleby, S. *Acta Crystallogr.* **1974**, *B30*, 2877. (f) Miller, G. P.; Jeon, I.; Faix, A. N.; Jasinski, J. P.; Athans, A. J.; Tetreau, M. C. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1777–1780.

(11) Olsson, K.; Almqvist, S. O. *Acta Chem. Scand.* **1969**, *23*, 3271–3272.

(12) Lu, D.; Rae, A. D.; Salem, G.; Weir, M. L.; Willis, A. C.; Wild, S. B. *Organometallics.* **2010**, *29*, 32–33.

derivatives until the discovery of the enormous stabilization of $(CH)_4(BH)_6$ (**1**, 104.7 kcal/mol at the MP2(fc)/6-31G* level) by Minyaev, Quapp, Subramanian, Schleyer, and Mo (MQSSM) in 1997.[13] The strikingly large energetic nonadditivity was based on the isodesmic comparison of **1** (which has the six borons in one molecule) with six 2-boraadamantanes, each having only one boron (see Table 1). The stabilization of **1** (and by implication of its B-alkyl derivatives)[6a−e] was ascribed to the cumulative result of the 24 hyperconjugative interactions between the adjacent σ_{CB} and the vacant boron p-orbitals in $(CH)_4(BH)_6$.[13] Herges et al.'s recent reinvestigation of the spherically aromatic T_d $C_{10}H_{12}^{2+}$ adamantdiyl dication identified the hyperconjugative contribution to its stabilization.[14] We have now extended these computational studies to many more main group element hexa- and tetra-heteroadamantanes **1**−**19** $(CH)_4(X)_6$ (X = BH, AlH, GaH, SiH_2, GeH_2, NH, PH, AsH, O, S, and Se) and $(CH_2)_6(Y)_4$ (Y = B, Al, Ga, SiH, GeH, N, P, and As). The computed energies of the isodesmic reactions for **1**−**19** (Table 1) show wide-ranging nonadditive behavior. In particular, the stabilizations of the Al and Ga systems are even larger than those with B. Indeed, the implied greater stability of **3** than **1** is consistent with Uhl's finding that $(GaR)_6(CR')_4$ (R′ = Et or Bu, R = Et) did not undergo the nido-carbaborane rearrangement observed on heating $[(BEt)_6(CMe)_4]$.[9]

Despite the lack of lone pairs and vacant valence orbitals, Si and Ge systems **7**−**10** also exhibit large stabilizations. Although more modest, the stabililization of the polyhetero N, P, As, and O derivatives are still considerable. In contrast, $(CH)_4S_6$ and $(CH)_4Se_6$ actually were destabilized (by 24.6 and 18.0 kcal/mol, Table 1). The reasons for this disparate behavior and the deviations from additivity, the subject of this paper, are not immediately apparent. The geometries have typical single bond lengths, and all valences are classical. The magnetic properties show that these cages are nonaromatic and lack continuous electron delocalization.

All geometries were local minima; the nonadditivity evaluations (Δ*H*, Table 1, corrected by unscaled zero-point vibrational energy) were computed at B3LYP/6-311+G**//B3LYP/6-311+G**[15] using Gaussian 03.[16] The small positive isotropic NICS(0)[17] (nucleus-independent chemical shifts) values computed at cage centers for **1**−**19** (Table 1) indicate that aromaticity is not responsible for the stabilization of these compounds. CMO-NICS[18] showed the negative NICS(0), −5.07 ppm for **4**, to be due to many small nonaromatic diatropic contributions of lower-lying MOs.

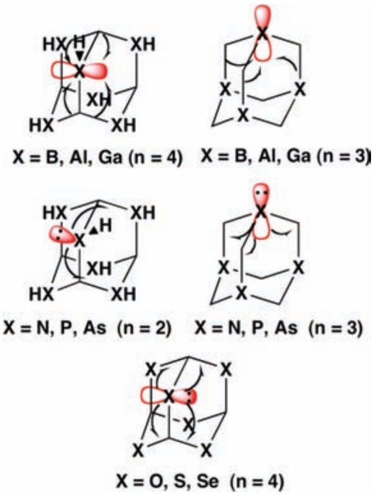


Figure 1. $\sigma_{CX}\rightarrow p_X$ (X = B, Al, Ga), $p_X\rightarrow\sigma^*_{CX}$ (X = N, P, As, O, S, Se) hyperconjugation demonstrations of **1**−**6**, **11**−**19**. *n* is the number of hyperconjugative interactions related to p orbitals of each X.

Figure 1 summarizes both anomeric (negative) $p_X\rightarrow\sigma^*_{CX}$[19] and regular $\sigma_{CX}\rightarrow p_X$ hyperconjugation. Thus, the boron derivatives **1** and **4** have 24 and 12 total interactions, respectively. Although the vacant p-orbital of boron is known to be the best group 13 acceptor,[20] the stabilizations of the Al and Ga analogues (**2**, **3**, **5**, and **6**) are even larger than those of **1** and **4**. The similarly large nonadditive stabilizations of the Si and Ge derivatives (**7**−**10**, Table 1) also point to the additional importance of another effect, electrostatic stabilization.

Wiberg et al.[3e] recognized that the presence of multiple electropositive or electronegative substituents on the same atom has major energetic consequences due to enhanced electrostatic interactions. Thus, $C(SiH_3)_4$ and CF_4 are stabilized (evaluated using the isodesmic equation $CX_4 + 3\ CH_4 \rightarrow 4\ CH_3X$ at MP3/6-311++G**//MP2/6-31G*) by 13.9 (X = SiH_3) and 49.3 (expt. 53.4) kcal/mol (X = F).[3e]

Like $C(SiH_3)_4$, the adamantane-based species **1**−**10** have multiple electropositive atoms bound to each carbon, three X's in **1**−**3**, **7**, and **8** and two X's in **4**−**6**, **9**, and **10**. Large carbon negative charges and enhanced Coulombic attractions with the positively charged heteroatoms result. The C and X charges (Table 1; note the values for Al and Ga in particular) provide direct evidence for the dominating role

---

(13) Minyaev, R. M.; Quapp, W.; Subramanian, G.; Schleyer, P. v. R.; Mo, Y. *J. Comput. Chem.* **1997**, *18*, 1792–1803.

(14) Bucher, G.; Köhler, F.; Herges, R. *J. Phys. Chem. A* **2008**, *112*, 9906–9910.

(15) Δ*H* values were checked at MP2 and G3 levels, where practicable, and were even larger due to the B3LYP branching error. See: (a) Wodrich, M. D.; Corminboeuf, C.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 3631–3634. (b) Wodrich, M. D.; Wannere, C. S.; Mo, Y.; Jaroeski, P. D.; Houk, K. N.; Schleyer, P. v. R. *Chem.—Eur. J.* **2007**, *13*, 7731–7744.

(16) Frisch, M. J. et al. Gaussian 03. (Full reference in the Supporting Information).

(17) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. R. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317–6318.

(18) Heine, T.; Schleyer, P. v. R.; Corminboeuf, C.; Seifert, G.; Reviakine, R.; Weber, J. *J. Phys. Chem. A* **2003**, *107*, 6470. The larger positive NICS(0) values in Table 1 are due to paratropic contributions from some of the higher lying MOs.

(19) Schleyer, P. v. R.; Kos, A. J. *Tetrahedron* **1983**, *39*, 1141–1150.

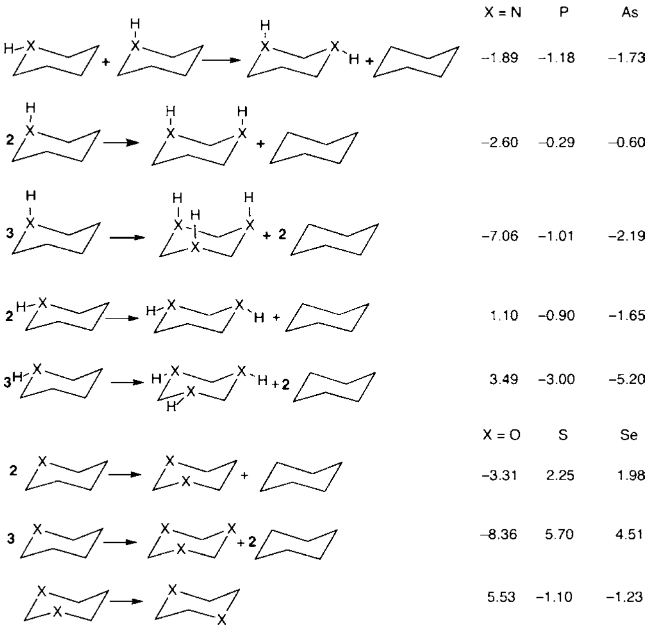
(20) Block localized wavefunction (BLW) evaluations of the hyperconjugation energies due to $\sigma_{CH}\rightarrow p_X$ (X = B, Al, Ga) interactions gave 5.42, 2.15, and 2.16 kcal/mol for staggered conformations of CH_3BH_2, CH_3AlH_2, and CH_3GaH_2, respectively, at B3LYP/6-31G(d)//B3LYP/6-311+G**. For the BLW method, see: (a) Mo, Y.; Peyerimhoff, S. D. *J. Chem. Phys.* **1998**, *109*, 1687. (b) Mo, Y.; Zhang, Y.; Gao, J. *J. Am. Chem. Soc.* **1999**, *121*, 5737. (c) Mo, Y.; Wu, W.; Song, L.; Lin, M.; Zhang, Q.; Gao, J. *Angew. Chem.* **2004**, *116*, 2020–2024. (d) Mo, Y. *J. Chem. Phys.* **2003**, *119*, 1300. (e) Mo, Y.; Song, L.; Lin, Y. *J. Phys. Chem. A* **2007**, *111*, 8291.

of electrostatic effects in the stabilization of **2**−**3** and **5**−**10**. Moreover, the larger stabilization of **2**, **3**, **5**, and **6** than **7**−**10** shows that $\sigma_{CX} \rightarrow p_X$ (X = Al, Ga) hyperconjugation also contributes significantly. Albeit smaller in magnitude, appreciable C (negative) − X (positive) charge differences are observed for X = P (**12, 15**) and As (**13, 16**) systems (Table 1).

MQSSM[13] pointed out that polysubstitution results in a large number of interactions. Although the energy of each one of these is modest individually, their cummulative effect is considerable; consequently, large deviations from "isodesmic" additivity result. This "multiplication" magnifies the sum of the electrostatic, steric, and hyperconjugative polyheteroadamantane interactions. Very large composite effects (Table 1) result.

Although O and N are the second and third most electronegative elements after F, **11**, **14**, and even **17** do not appear to behave like CF_4 electrostatically.[3c,e] This is indicated by the much smaller C and X charges in Table 1. The main stabilizing contribution to **11**, **14**, and **17** is "negative hyperconjugation" ("anomeric effect"),[19] involving $lp_X \rightarrow \sigma^*_{CX}$ (X = N, O, Figure 1).

Scheme 1. Evaluations of Nonadditive 1,3- (or 1,4-) X•••X Interactions in Di- and Trisubstituted Cyclohexanes (B3LYP/6-311+G** + ZPE)



Consistent with our previous reports,[3b−d] hyperconjugation effects involving second- and third-row elements do not disappear but are significantly attenuated relative to their first-row counterparts. Di- and trisubstituted cyclohexanes (see Scheme 1) model the 1,3-X•••X (X = N, P, As) interactions in **11**−**13** nicely. Note that the nonadditivity values (based on monosubstituted rings) of the 1,3,5-trisubstituted cyclohexanes are approximately three times those of their 1,3-disubstituted analogues. The expected stabilizations of **11**−**13** based on transferability of the disubstituted cyclohexane data and on the relative axial (*a*) or equatorial (*e*) hydrogen configurations of **11**−**13** (all have six *ae*'s, three *aa*'s, and three *ee*'s) are 15.8 kcal/mol for **11** [i. e., (−1.89 × 6) + (−2.60 × 3) + (1.10 × 3)], 10.7 kcal/mol for **12**, and 17.1 kcal/mol for **13**. The data in Table 1 (9.72, 11.65, 18.78 kcal/mol, respectively) are reasonably consistent, as ring strain (verified in other models) may reduce the value for **11**.

Why are **18** and **19** destabilized? The electrostatic effect should be small since the electronegativities of C, S, and Se are similar. However, each S(Se) has two lone pairs, and the 1,3-S•••S (Se•••Se) distances, 3.088 Å (3.338 Å), shorter than the van der Waals separations, 3.60 Å (3.80 Å), indicate steric repulsions. (The nonadditive energies shown in Scheme 1 agree.) Houk et al. investigated the interactions involving the S lone pairs and neighboring σ bonds in the complete set of polythiaadamantanes very thoroughly recently but did not address the nonadditivity issue.[21]

Although 1,3-dioxane is favored over its 1,4-isomer by 5.5 kcal/mol (expt. 5.5 kcal/mol), both 1,3-dithiacyclohexane and 1,3-diselenacyclohexane are 1.1 and 1.2 kcal/mol less stable, respectively, than their 1,4-disubstituted counterparts (Scheme 1). Based on the isodesmic reactions involving thia- and selenacyclohexane, 1,3-S•••S and Se•••Se repulsions destabilize 1,3-dithia- and 1,3-diselenacyclohexane by 2.3 and 2.0 kcal/mol, respectively. Thus, 12 such 1,3-interactions are expected to destabilize **18** and **19** by 27.6 and 24.0 kcal/mol, compared to the respective directly computed 24.6 and 18.0 kcal/mol values (Table 1). Such repulsions are absent or much reduced by the hydrogen-substituted heteroatoms of the pnictide species, which have only one lone pair on each heteroatom, and the stabilizing hyperconjugative and electrostatic effects dominate. The behavior of the heteroadamantanes is mirrored by that of the Scheme 1 cyclohexane-based set.

In conclusion, isodesmic reaction energies have identified remarkably large (up to 178 kcal/mol!) nonadditivities in heteroadamantanes **1**−**19**. The stabilization and destabilizations are due to the interplay among hyperconjugation (dominating in B, N, O species), electrostatic (Al, Ga, Si, Ge, P, As), and strain (S and Se lone pair repulsion) effects.

Acknowledgment. We thank the China Scholarship Council (CSC) for Y.W.'s study fellowship at the University of Georgia, the National Science Foundation (Grant No. CHE-0716718) for financial support, and U. Salzner for her comments and interest.

Supporting Information Available: Structural data, NBO charges, and NICS(0) for **1**−**19** and their monosubstituted reference molecules. The information is available free charge via the Internet at http://pubs.acs.org.

OL1002187

---

[21] Norton, J. E.; Briseno, A. L.; Wudl, F.; Houk, K. N. *J. Phys. Chem. A* **2006**, *110*, 9887–9899.