Pergamon

Tetrahedron 54 (1998) 11381–11386

TETRAHEDRON

Thermodynamic Rearrangement of the Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane Skeleton

Kata Mlinarić-Majerski,*† and Jelena Veljković

Department of Chemistry, Rudjer Bošković Institute, P. O. Box 1016, 10000 Zagreb, Croatia

Alan P. Marchand*§ and Bishwajit Ganguly

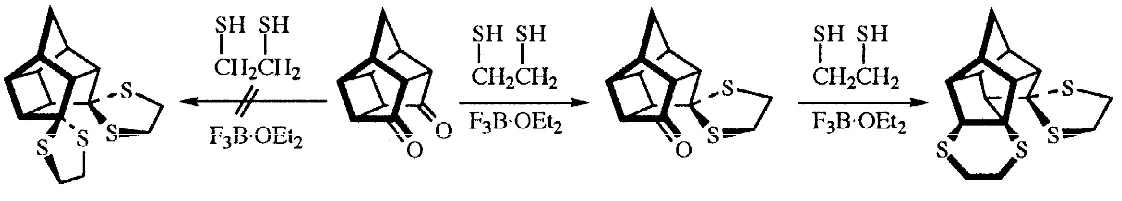
Department of Chemistry, University of North Texas, Denton, Texas 76203-5070

Received 14 April 1998; revised 26 June 1998; accepted 6 July 1998

Abstract:. Reaction of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (**1**) with ethanedithiol, when performed in the presence of a Lewis acid catalyst (F_3B-OEt_2), afforded the corresponding mono(ethylene dithioacetal), **2**, along with 7,8-[(thioethano)thio]pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-11-one mono(ethylene dithioacetal) (**3**). Raney nickel reduction of **2** resulted in hydrogenolysis of both the dithioacetal moiety and the cyclobutane ring in **2** and led to the formation of a complex mixture of products (**7-10**). In contrast to this result, Raney nickel reduction of **3** afforded a single product, i.e., 7,8-[(thioethano)thio]pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**11**) in 35% yield.

As a part of program that is concerned with the synthesis and chemistry of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (PCU) derivatives,[1] we recently studied the Lewis acid promoted reaction of PCU-8,11-dione (**1**)[2] with 1,2-ethanedithiol (Scheme 1). In our hands, the reaction of **1** with 1,2-ethanedithiol, when performed in the presence of F_3B-OEt_2 (ratio **1** : 1,2-ethanedithiol : F_3B-OEt_2 = 1 : 2.4 : 1.2), afforded the corresponding mono(ethylene dithioacetal) (**2**, 71% yield) along with a small amount of a tetrathio compound, **3**.[3] When the amount of F_3B-OEt_2 was increased (ratio **1** : 1,2-ethanedithiol : F_3B-OEt_2 = 1 : 2.4 : 3.0), **3** became the sole reaction product. The corresponding bis(ethylene dithioacetal), i.e., **4**, was not observed among the products of this reaction.

Scheme 1



4 (not formed) **1** **2** **3**

---

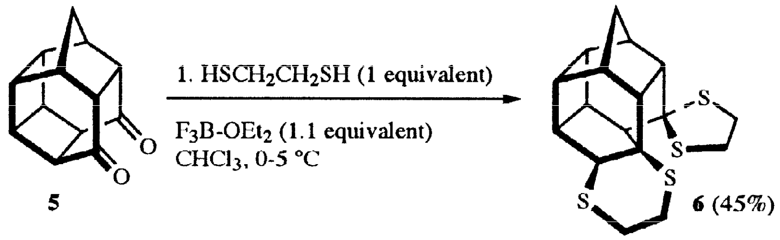
† To whom correspondence should be addressed. E-mail: majerski@rudjer.irb.hr

§ To whom correspondence should be addressed. E-mail: fg83@jove.acs.unt.edu

PII: S0040-4020(98)00680-2

A similar rearrangement was reported previously in connection with the attempted conversion of hexacyclo[6.5.0.0^{2,7}.0^{4,12}.0^{5,10}.0^{9,13}]tridecan-3,6-dione (**5**) into its corresponding mono(dithioacetal). Unexpectedly, in the presence of $F_3B \cdot OEt_2$ catalyst, the reaction of **5** with ethanedithiol proceeded with concomitant skeletal rearrangement to afford **6** (45% yield; see Scheme 2).[4] Relief of steric strain was cited as a possible driving force for this rearrangement.[4]

Scheme 2

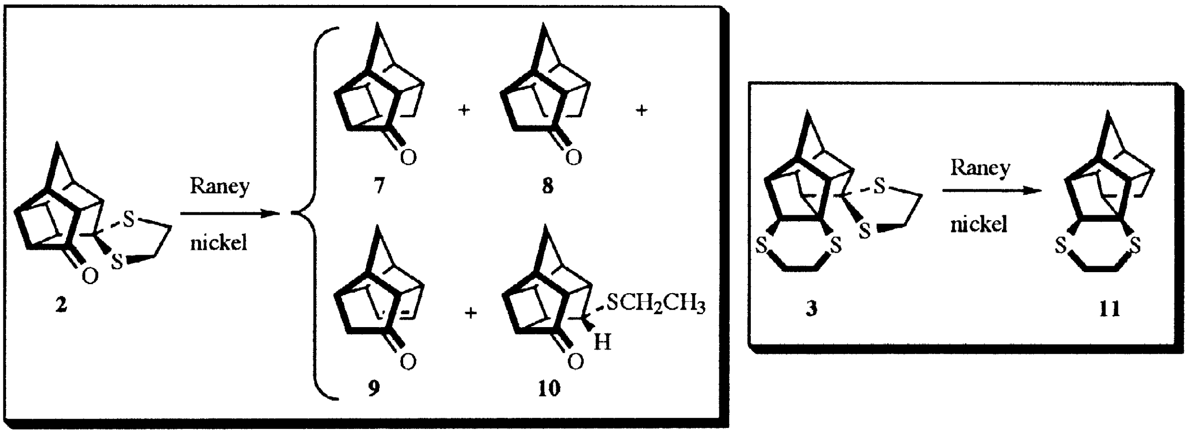


Similarly, relief of steric strain might also provide a driving force for the rearrangement of **1** to **3** that occurred during attempted $F_3B\text{-}OEt_2$ promoted conversion of **1** into **4**. In this regard, it should be noted that **3** is a derivative of D_3-trishomocubane; the parent hydrocarbon has been shown to be the pentacyclic $C_{11}H_{14}$ "stabilomer" (i.e., the most stable pentacyclic $C_{11}H_{14}$ isomer).[5]

The structure of **3** was established via analysis of its IR, ^1H NMR, and ^{13}C NMR spectra and also by chemical means. Thus, reduction of **3** with Raney nickel in ethanol afforded **11** (Scheme 3) in 35% yield. The mass spectrum of **11** contains the molecular ion at m/z 236 (relative intensity 100%), thereby indicating that reduction of **3** proceeds with concomitant loss of the dithioethylene group. In addition, the structure suggested for **11**, i.e., 7,8-[(thioethano)thio]pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane, is consistent with its IR, ^1H NMR, and ^{13}C NMR spectra (see the Experimental Section).

By way of contrast, treatment of dithioacetal **2** with Raney nickel afforded a mixture of four ketones, i.e., **7-10** (Scheme 3), in 75% yield. The IR and NMR spectral data for **7**, **8**, and **9** are in accord with spectral data that have been reported previously[6,7] The structure suggested for **10** is consistent with its IR, ^1H NMR, and ^{13}C NMR spectra (see the Experimental Section). On the basis of these results, we conclude that Raney nickel reduction of **2** results in desulfurization with concomitant hydrogenolysis of its cyclobutane ring.[8-10]

Scheme 3



The behavior noted for **2** is in accord with the known propensity of pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]-undecan-8,11-dione (**1**) to afford the corresponding mono- rather than bis-ethylene acetal.[6] Attempts to introduce bulky substituents frequently result in concomitant skeletal rearrangement of the cage system and lead exclusively to the formation of the corresponding, functionalized D_3-trishomocubanes.[11]

Molecular mechanics and ab initio calculations have been performed[12] in an effort to examine the relative stabilities of the sulfur-containing cage systems reported herein and also to attempt to identify and to evaluate the factors responsible for the exclusive formation of **3** from **2**. For comparison, the corresponding calculations have been performed for the parent pentacyclic $C_{11}H_{14}$ hydrocarbon systems from which **3** and **4** are derived [i.e., pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane (**12**) and pentacyclo[6.3.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane (i.e., "D_3-trishomocubane", **13**), respectively]. The results thereby obtained are summarized in Table 1.

Table 1. Results of molecular mechanics and ab initio calculations.[12]

Compound	**Strain Energy**[a] **(kcal-mol^{-1})**	**RHF/6-31G***[b] **(kcal-mol^{-1})**
3	47.4 (44.2)[c]	0.0[d] (0.0)[c,d]
4	67.1 (57.9)[c]	20.2[d] (8.2)[c,d]

[a]Calculated by using PCMODEL, version 4.0.[12a] [b]Calculated by using GAUSSIAN94.[12b]
[c]Calculated energies of the corresponding hydrocarbon. [d]Calculated relative energies.

The results of these molecular mechanics calculations indicate that bis(ethylene dithioacetal) **4** contains *ca.* 19.7 kcal-mol^{-1} additional strain energy *vis-à-vis* **3**. This anticipated accrual of steric strain in **4** appears to effectively prevent its formation via Lewis acid promoted reaction of **2** with ethanedithiol. Indeed, a comparable strain energy differential exists for the corresponding parent hydrocarbons; thus, **12** contains *ca.* 13.7 kcal-mol^{-1} additional strain energy relative to **13**. It thus appears that in addition to the difference between the inherent stabilities of the parent carbocyclic ring systems, there is an additional *ca.* 6 kcal-mol^{-1} strain energy present in **4** *vis-à-vis* **3**. This additional strain in **4** *vs.* **3** may arise from deleterious steric interactions that occur between the sulfur atoms situated on adjacent rings, a situation which appears to be more serious in the former compound.

The foregoing conclusions receive additional support from the results of ab initio calculations. Thus, the results of calculations performed at the HF/6-31G* level of theory suggest that **4** contains *ca.* 20.2 kcal-mol^{-1} additional strain energy *vis-à-vis* **3**, while **12** contains *ca.* 8.2 kcal-mol^{-1} additional strain energy relative to **13** (see Table 1). In addition, the observed difference in reactivity of **1** and **5** with ethanedithiol has been examined further at the HF/6-31G* level of theory. It was noted above that whereas **1** could be converted easily into its corresponding mono(ethylene dithioacetal) (i.e., **2**), the same is not true for **5**.[4] The results of HF/6-31G* calculations performed for hexacyclo[6.5.0.$0^{2,7}$.$0^{4,12}$.$0^{5,10}$.$0^{9,13}$]tridecane (**14**) and hexacyclo[6.5.0.$0^{3,7}$.$0^{4,12}$.$0^{8,10}$.$0^{9,13}$]tridecane (**15**) (i.e., the "parent hydrocarbons" that correspond to **5** and **6**, respectively) reveal that **15** is more stable than **14** by *ca.* 19.2 kcal-mol^{-1}. Since we have seen that **13** is preferred thermodynamically *vis-à-vis* **12** by only *ca.* 8.2 kcal-mol^{-1}, we conclude that a cyclobutane σ-bond in **5** is likely to be more susceptible to

Wagner-Meerwein rearrangment than is the corresponding σ-bond in **2**. This conclusion is supported by the experimental observations reported herein and in an earlier publication.[4]

Summary and Conclusions. A novel tetrathio cage compound, **3**, was obtained in good yield via Lewis acid promoted reaction of **1** with excess ethanedithiol. The structure of **3** was established via analysis of its IR, ^{1}H NMR, and ^{13}C NMR spectra. Based upon the results of molecular mechanics and ab initio calcualtions performed at the HF/6-31G* level of theory,[12] it seems likely that the observed propensity of **2** to react with ethanedithiol in the presence of $F_3B{\cdot}OEt_2$ catalyst to afford **3** rather than **4** can be accounted for in terms of (i) anticipated accrual of steric strain concomitant with the formation of **4** from **2** and (ii) anticipated relief of steric strain concomitant with skeletal rearrangement that accompanies the formation of **3** from **2**. Raney nickel reduction of **2** afforded a complex mixture of products (**7-10**). However, the corresponding reduction of **3** afforded a single product, **11**, in modest yield.

Experimental Section

The purity of all compounds was determined by GLC and/or NMR spectral analysis. GLC analyses were performed by using a Varian 3300 gas chromatograph on capillary column DB-210. ^{1}H and ^{13}C NMR spectra were obtained on Varian Gemini 300 spectrometer. IR spectra were recorded on a Perkin-Elmer M-297 spectrophotometer. Melting points are determined on a Kofler apparatus and are uncorrected. Elemental microanalytical and high-resolution mass spectral (HRMS) data were obtained by personnel at the Central Analytical Laboratory of the Rudjer Boskovic Institute, Zagreb, Croatia.

Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8,11-one Mono(ethylene dithioacetal) (2). A solution of **1** (3.20 g, 18.4 mmol) and ethanedithiol (1.7 mL, 20 mmol) in $CHCl_3$ (80 mL) was cooled to 0 °C via application of an external ice-water bath. To this cooled solution was added dropwise with stirring $F_3B{\cdot}OEt_2$ (2.5 mL, 20 mmol). After all of the $F_3B{\cdot}OEt_2$ had been added, the resulting mixture was stirred at 0 °C for 0.5 h. The external cold bath then was removed, and the reaction mixture was allowed to warm gradually to ambient temperature with stirring overnight. The reaction mixture was poured into 10% aqueous NaOH (400 mL). The layers were separated, and the aqueous layer was extracted with $CHCl_3$ (3 x 100 mL). The combined organic layers were washed with water (50 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. The oily residue thereby obtained crystallized slowly when allowed to stand at ambient temperature. The resulting solid was washed with pentane and then air-dried to afford **2** (3.24 g, 71%) as a colorless microcrystalline solid: mp 96-98 °C (lit.[7] mp 85-86 °C); IR (KBr) 2980 (m), 2950 (m), 2930 (m), 2860 (m), 1730 (s), 1425 (w), 1140 (w), 900 (w), 820 cm^{-1} (m); ^{1}H NMR ($CDCl_3$) δ 1.58 (A*B*, J_{AB} = 11.2 Hz, 1 H), 1.94 (*A*B, J_{AB} = 11.2 Hz, 1 H), 2.42-2.84 (m, 4 H), 2.87-3.00 (m, 2 H), 3.04-3.15 (m, 2 H), 3.15-3.33 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 34.1 (d), 37.7 (t), 37.8 (t), 39.7 (t), 42.7 (d), 43.5 (d), 44.0 (d), 49.3 (d), 51.0 (d), 52.6 (d), 60.1 (d), 73.8 (s), 216.1 (s).

7,8-[(Thioethano)thio]pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-11-one Mono(ethylene dithioacetal) (3). A solution of **1** (174 mg, 1.0 mmol) and ethanedithiol (0.2 mL, 2 mmol) in $CHCl_3$ (8 mL) was cooled to 0 °C via application of an external ice-water bath. To this cooled solution was added dropwise with stirring $F_3B{\cdot}OEt_2$ (0.20 mL, 1.5 mmol). After all of the $F_3B{\cdot}OEt_2$ had been added, the resulting mixture was stirred at 0 °C for 2 h. Then, an additional quantity of $F_3B{\cdot}OEt_2$ (0.20 mL, 1.5 mmol) was added dropwise with stirring, after which the resulting mixture was stirred at 0 °C for 2 h. The external cold bath then was removed, and the reaction mixture was allowed to warm gradually to ambient temperature with stirring overnight. The reaction mixture was poured into 10% aqueous NaOH (40 mL). The layers were separated, and the aqueous layer was extracted with $CHCl_3$ (3 x 20 mL). The combined organic layers were washed with water (30 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. Crude **3** (236 mg, 72%) was thereby obtained as a colorless solid. Analytically pure **3**, mp 152-155 °C, was obtained as a colorless microcrystalline solid via column chromatographic purification of this material on silica gel by eluting with 1:1 CH_2Cl_2-pentane; IR (KBr) 3000 (m), 2960 (m), 2940 (m), 2910 (m), 2900 (m), 2870 (m), 1410 (m), 1270 (m), 1240 (m), 1200 (w), 800 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.37 (A*B*, J_{AB} = 10.8 Hz, 1 H), 1.44 (*A*B, J_{AB} = 10.8 Hz, 1 H), 2.14-2.24 (m, 1 H), 2. 24-2.34 (m, 1 H), 2.36-2.54 (m, 3 H), 2.60-3.42 (m, 11 H); ^{13}C NMR ($CDCl_3$) δ 26.9 (t), 27.0 (t), 32.8 (t), 37.2 (t), 40.5 (t), 44.1 (d), 46.5 (d), 48.1 (d), 48.9 (d), 49.1 (d), 50.5 (d), 57.8 (s), 61.3 (d), 64.2 (d), 75.2 (s). HRMS Calcd for $C_{15}H_{18}S_4$: M_r^+ 326.02914. Found: M_r^+ 326.05444. Anal. Calcd for $C_{15}H_{18}S_4$: C, 55.17; H, 5.55. Found: C, 55.19; H, 5.48.

Reduction of 2 with Raney Nickel. To a solution of **2** (2.01 g, 8.04 mmol) in EtOH (100 mL) was added Raney nickel (23.8 g, excess), and the resulting mixture was refluxed with stirring for 40 h. The reaction mixture was allowed to cool gradually to ambient temperature and then was filtered to remove spent catalyst. The filtrate was concentraed *in vacuo* to a final volume of 20 mL. Water (60 mL) was added, and the resulting aqueous suspension was extracted with Et_2O (3 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The oily residue (965 mg) was subjected to GLC analysis (DB-210 column, 150-200 °C), which revealed the presence of **7-10** (product ratio **7** : **8** : **9** : **10** = 3 : 3 : 1 : 1) along with a small amount of unreacted (recovered) **2**.

The mixture of reaction products was separated via column chromatography on alumina (activity grade II/III) by using a 5-20% Et_2O-pentane gradient elution scheme. The first chromatography fraction, when concentrated *in vacuo*, afforded a 1:1 mixture of **7** and **8** (275 mg, 21%).[7] The ^1H NMR and ^{13}C NMR spectra of the mixture of **7** and **8** corresponded with the sum of the corresponding spectra that have been reported previously for the individual pure compounds.[7]

Workup of the second chromatography fraction afforded **9** (51 mg, 4%). The IR and ^1H NMR spectra of the material thereby obtained were essentially identical to the corresponding spectra reported previously for authentic **9**;[6] ^{13}C NMR ($CDCl_3$) δ 33.6 (t), 38.2 (d), 42.3 (t), 46.1 (d), 49.9 (d), 51.7 (d), 55.9 (d), 59.5 (d), 136.3 (d), 137.7 (d), 221.2 (s). HRMS Calcd for $C_{11}H_{12}O$: M_r^+ 160.088815. Found: M_r^+ 160.089028.

Workup of the third chromatography fraction afforded **10** (72 mg, 4%) as a colorless oil; IR (neat) 2960 (s), 2860 (m), 1740 (s), 1450 (w), 1260 (m), 1075 (w), 965 (w), 915 (w), 745 cm^{-1} (w); ^1H NMR ($CDCl_3$) δ 1.24 (t, J = 7.2 Hz, 3 H), 1.52 (*A*B, J_{AB} = 11.0 Hz, 1 H), 1.91 (A*B*, J_{AB} = 11.0 Hz, 1 H), 2.38-2.47 (m, 1 H), 2.52 (q, J = 7.2 Hz, 2 H), 2.57-3.14 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 14.6 (q), 25.8 (t), 35.6 (d), 37.4 (t), 41.6 (d), 41.8 (d), 41.9 (d), 43.0 (d), 46.4 (d), 47.8 (d), 50.1 (d), 52.2 (d), 216.5 (s). HRMS Calcd for $C_{13}H_{16}SO$: M_r^+ 220.092187. Found: M_r^+ 220.102396.

Raney-Nickel Reduction of 3. To a solution of **3** (326 mg, 1.0 mmol) in EtOH (14 mL) was added Raney nickel (3.0 g, excess), and the resulting mixture was refluxed with stirring for 40 h. The reaction mixture was allowed to cool gradually to ambient temperature and then was filtered to remove spent catalyst. The filtrate was concentraed *in vacuo* to a final volume of 7 mL. Water (20 mL) was added, and the resulting aqueous suspension was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. Compound **11** (84 mg, 35%) was thereby obtained as a colorless microcrystalline solid: mp 50-52 °C; IR (KBr) 2970 (s), 2950 (s), 2860 (m), 1460 (w), 1410 (m), 1285 (s), 1000 (m), 910 (m), 815 cm^{-1} (m); ^{1}H NMR ($CDCl_3$) δ 1.28 (*A*B, J_{AB} = 10.5 Hz, 1 H), 1.42 (*A*B, J_{AB} = 8.9 Hz, 1 H), 1.45 (A*B*, J_{AB} = 8.9 Hz, 1 H), 1.72 (A*B*, J_{AB} = 10.5 Hz, 1 H), 2.00-2.26 (m, 6 H), 2.64-2.94 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 25.6 (t), 28.2 (t), 31.7 (t), 32.8 (t), 41.6 (d), 46.7 (d), 46.8 (d), 47.3 (d), 47.5 (2C, d), 51.1 (d), 53.1 (d), 57.0 (s). HRMS Calcd for $C_{13}H_{16}S_2$: M_r^+ 236.069344. Found: M_r^+ 236.072520.

Acknowledgment. We thank the Robert A. Welch Foundation (Grant B-0963 to A. P. M.) and the Croatian-American Joint Fund, in cooperation with the Croatian Ministry of Science and Technology and the U. S. National Science Foundation (Grant JF-141 to K. M. and A. P. M.), for financial support of this study.

References and Footnotes

1. (a) Marchand, A. P. in *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed; JAI: Greenwich, CT Vol. 1. **1989**, pp 357. (b) Marchand, A. P. *Aldrichimica Acta* **1995**, *28*, 95.
2. Marchand, A. P.; Allen, R. W. *J. Org. Chem.*, **1974**, *39*, 1596.
3. A single mono(ethylene dithioacetal), **2**, was obtained via reaction of **1**, ethanedithiol, and F_3B-OEt_2 (molar ratio 1 : 1.1 : 1.1).
4. Kashyap, R. P.; Deshpande, M. N.; Rajapaksa, D.; Marchand, A. P.; Watson, W. H. *J. Chem. Crystallography* **1995**, *25*, 573.
5. (a) Kent, G. J.; Godleski, S. A.; Osawa, E.; Schleyer, P. von R., *J. Org. Chem.* **1977**, *42*, 3852. (b) Osawa, E.; Musso, H., *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 1.
6. Eaton, P. E.; Cassar, L.; Hudson, R. A.; Hwang, D.R., *J. Org. Chem.* **1976**, *41*, 1445.
7. Lerman, B. M.; Galin, F. Z.; Umanskaya, L. I.; Tolstikov, G. A., *Zh. Org. Khim.* **1978**, *14*, 2536.
8. Hydrogenolyses of cyclobutane rings in homocubane[9] and in basketane[10] have been reported.
9. (a) Osawa, E.; Schneider, I.; Toyne, K. J.; Musso, H. *Chem. Ber.* **1986**, *119*, 2350. (b) Stober, R.; Musso, H.; Osawa, E. *Tetrahedron* **1986**, *41*, 1757. (c) Toyne, K. J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1346.
10. (a) Sasaki, N. A.; Zunker, R.; Musso, H. *Chem. Ber.* **1973**, *106*, 2992. (b) Osawa, E.; Schleyer, P. von R.; Chang, L. W. K.; Kane, V. V. *Tetrahedron Lett.* **1974**, 4189.
11. Marchand, A. P.; Sharma, G. V. M.; Annapurna, G. S.; Pednekar, P. R., *J. Org. Chem.*, **1987**, *52*, 4784.
12. (a) Molecular mechanics calculation were performed by using the computer programs PCMODEL, version 4.0 (available from Serena Software, Bloomington, IN). (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; AlLatham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J . J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94*; Gaussian, Inc.: Pittsburgh, PA, 1995.