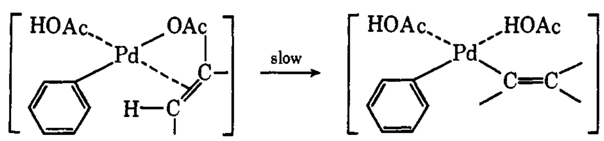

should exhibit a primary kinetic isotope effect when coupled with benzene.[11] We have carried out the palladium(II) acetate effected coupling of benzene with styrene and styrene-β,β-d_2 under both competitive and independent conditions and have found only a small isotope effect. The independent reactions give $K_H/K_D = 1.25 \pm 0.08$. Precise interpretation of mass spectrometry data of a competitive run is complicated by the presence of a small amount of styrene-β-d_1 in the starting material, but a value of $K_H/K_D \approx 1$ is indicated. While rare examples of reactions presumably involving C–H bond cleavage in their rate-determining steps are known which exhibit kinetic isotope effects of less than 2,[13] primary kinetic hydrogen isotope effects are generally in the range of 2–9. A value as low as that observed here is indicative of a secondary isotope effect and suggests that cleavage of the styrene-β-hydrogen bond is not involved in the rate-determining step of olefin arylation.

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[11] Moritani and coworkers have recently reported the reaction between benzene, styrene-β,β-d_2, and palladium(II) acetate, [2] but their concern was with establishing the absence of a hydride shift in the mechanism rather than in determining an isotope effect.

[12] S. Danno, I. Moritani, and Y. Fujiwara, *Chem. Commun.*, 610 (1970).

[13] F. H. Westheimer, *Chem. Rev.*, 61, 265 (1961), and references therein.

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Limitations of the Use of Conformational Energies of Substituents in Bicyclo[2.2.1]heptane[1,2]

Sir:

The determination of the conformational energies of substituents attached to cyclohexane has been a central goal of conformational analysis for many years.[3,4] For most substituents, the values have been determined by a variety of techniques both direct and indirect, by physical and chemical methods and in a number of phases over a considerable range of temperatures. In light of the effort expended in obtaining conformational energies, it would be useful if these quantities could be utilized in at least a qualitative manner in other ring systems. In this report, the applicability of conformational energies in the widely studied bicyclo[2.2.1]heptane system is examined for the substituents methyl, hydroxyl, carbomethoxy, and nitro.

2-Methylbicyclo[2.2.1]heptane was equilibrated directly at 300° over a Pd/C catalyst in a sealed tube. The calculated ΔG value given in Table I represents the stability of the exo over the endo isomer. For comparison, the conformational energy of methyl on cyclohexane is also given. An equilibration in the 200–300° range yields the most directly comparable value.[5] However, the value of 1.70 kcal/mol is one of the best established quantities and is apparently essentially an enthalpy dominated term.[4] Using the methyl group as a reference substituent, the generalization could be made that the conformational energies in bicyclo[2.2.1]heptane are approximately one-half those of cyclohexane. However, equilibration of bicyclo[2.2.1]heptan-2-ol using Raney nickel in refluxing isopropyl alcohol yields a free-energy difference of 1.05 kcal/mol[6,7] which is larger than that of the methyl group. A direct comparison with the value for the cyclohexane ring determined by Eliel[8] under the same conditions is given in Table I. In the case of hydroxyl, the conformational energy is larger in bicyclo[2.2.1]heptane than in cyclohexane.

Table I. Comparison of Conformational Energies (Kilocalories per Mole)

Group	Cyclohexane	Bicyclo-[2.2.1]heptane	T, °C
CH_3	1.70	0.89	300
OH	0.95	1.05	82
CO_2CH_3	1.27	0.65	75
NO_2	1.20	1.38	100

A comparison of the trigonal groups carbomethoxy and nitro in both cyclohexane and bicyclo[2.2.1]heptane is given in Table I. The values in bicyclo[2.2.1]heptane were determined using methanol and sodium methoxide for the carbomethoxy group and *tert*-butyl alcohol and potassium *tert*-butoxide for the nitro group. These conditions are the same for the cyclohexane compounds.[9–11] If carbomethoxy were used as a reference substituent for the two ring systems, the generalization could again be made that conformational energies of bicyclo[2.2.1]heptane are one-half those of cyclohexane. However, the nitro group is clearly larger than expected in bicyclo[2.2.1]heptane.

A rationale for the larger than expected conformational energies of hydroxyl and nitro in bicyclo[2.2.1]heptane when compared to methyl and carbomethoxy must involve detailed force-field calculations. Qualitatively an argument based on bond lengths and steric environments of the axial position of cyclohexane compared to the endo position of bicyclo[2.2.1]heptane provides some insight. The shape of the potential

[1] Part XVI in a series entitled Conformational Analysis. Conformational Analysis. XV: R. J. Ouellette, D. Baron, J. Stolfo, A. Rosenblum, and P. Weber, *Tetrahedron*, submitted for publication.

[2] This research was supported by Grant No. GP-9231 from the National Science Foundation.

[3] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, pp 36–128, 436–442.

[4] J. A. Hirsch, *Top. Stereochem.*, 1, 199 (1967).

[5] Unpublished results of W. Szkrybalo, F. A. Van Catledge, and N. L. Allinger cited in ref 4.

[6] This value is in good agreement with one of 1.03 kcal/mol calculated by these authors from the data of Wilcox[7] obtained at 100° using aluminum isopropoxide.

[7] C. T. Wilcox, Jr., M. Sexton, and M. F. Wilcox, *J. Org. Chem.*, 28, 1079 (1963).

[8] E. L. Eliel and E. C. Gilbert, *J. Amer. Chem. Soc.*, 91, 5487 (1969).

[9] R. J. Ouellette and G. E. Booth, *J. Org. Chem.*, 31, 587 (1966).

[10] The value for carbomethoxy is in good agreement with that of 1.29 kcal/mol calculated from the thermodynamic parameters of Eliel.[11]

[11] E. L. Eliel and M. C. Rees, *J. Amer. Chem. Soc.*, 90, 1560 (1968).

energy curve for a substituent in a ring system will be a sum of all of the interactions customarily considered in force-field calculations. If the curve is considered as a function of some variable and, of course, artificial bond distance between the ring and the substituent, it is not unreasonable that the curve for one ring system may cross that of another ring system. The ordering of steric sizes will depend on the actual bond length and therefore the order of conformational energies of substituents may become reversed. In the endo position of bicyclo[2.2.1]heptane, the van der Waals interactions will be more serious at short distances than in the axial position of cyclohexane. Furthermore, bond bending, bond stretching, and torsional changes may be more easily accomplished in cyclohexane than the strained, relatively constrained bicyclo[2.2.1]heptane. The carbon–oxygen bond distance is approximately 0.1 Å shorter than the carbon–carbon bond distance, and as a consequence the shape of the potential energy curves for hydroxyl and methyl could indeed cross. In a similar manner, the carbon–nitrogen bond of nitro compounds is expected to be shorter than the carbon–carbon bond of carbomethoxy compounds, and the potential energy curves may again cross.

From these observations, it can be concluded that using conformational energies derived from cyclohexane in other ring systems is unwise in even a qualitative sense and may lead to seriously incorrect interpretations of data. Force-field calculations and experimental determinations of representative substituents such as a methyl group in a variety of bicyclic ring systems are in progress.

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Elimination Reactions of Cyclooctylammonium Salts in Liquid Ammonia

Sir:

On the basis of deuterium labeling and comparative rate studies, Sicher and coworkers[1] have suggested that the Hofmann elimination reaction with medium-ring compounds afforded *cis*-olefins by an anti mechanism and *trans*-olefins by a syn mechanism (syn–anti dichotomy). Using specifically labeled *cis*- and *trans*-*N*,*N*,*N*-trimethylcyclooctylammonium-*2*-d_1 hydroxides, Coke and Mourning[2] found that indeed *trans*-cyclooctene is formed by a 100% syn elimination with syn k_H/k_D = 1.94. The *cis*-olefin, however, was apparently formed by a 51% syn and 49% anti mechanism with an anti k_H/k_D = 2.64 (calculated). In an investigation of the modified Hofmann elimination, Wittig and Polster[3] found that reaction of trimethylcyclooctylammonium bromide with phenyllithium in diethyl ether gave an olefin mixture containing 80% *cis*-cyclooctene, but that with potassium amide in liquid ammonia the *trans*-olefin predominated (85%). The striking difference in product composition and the high proportion of a *cis*-olefin suggested the intervention of an α', β (ylide) mechanism. Despite the extensive investigation of the Hofmann elimination reaction with alicyclic derivatives,[4] a definitive study of these reactions in liquid ammonia has not appeared. We wish to report several examples of reactions of trialkylcyclooctylammonium salts in liquid ammonia using potassium amide as the base that proceed by a syn α', β mechanism.[5a]

The elimination reaction of *N*,*N*,*N*-dimethylbenzyl-*cis*-cyclooctylammonium-*2*-d_1 chloride (**1**) in liquid ammonia (−33°) using KNH_2 as the base afforded a mixture of olefins that was 95.4% *cis*-cyclooctene and 4.6% *trans*-cyclooctene. Since elimination with the trans *2*-d_1 salt **2** proceeded without loss of deuterium, the formation of *cis*-olefin must proceed by a 100% syn pathway. The dimethylbenzylamine recovered from **1** contained *ca.* 66% of the deuterium lost by syn elimination (syn k_H/k_D = 1.47). However, approximately 12% of the deuterium initially present in **1** could not be accounted for in the products isolated from the reaction because of exchange.[5b] On the basis of these data a minimum of 64% of the *cis*-olefin must arise by an α', β elimination. Incorporation of *ca.* 1.0% deuterium in the dimethylbenzylamine derived from **2** suggests that the *trans*-cyclooctene is also formed by an intramolecular ylide pathway.

Similarly, the data in Table I show that the *trans*-olefin from **3** and the *cis*-olefin from **4** are both formed by a syn elimination without loss of deuterium (within experimental error). The observation of both *cis*- and *trans*-olefins being derived completely by a syn mechanism is unique, and we can therefore directly measure the isotope effect for the formation of both olefins. In the formation of *trans*-cyclooctene from **4** loss of hydrogen results in *trans*-cyclooctene-d_1 (85.5%) and loss of deuterium results in *trans*-cycloocente-d_0 (14.5%) and a syn k_H/k_D = 5.89 can be calculated from these data. The difference in isotope effects for the formation of *trans*-cyclooctene and *cis*-cyclooctene (syn k_H/k_D = 2.07) is significant since it has been assumed that[2] the isotope effects for the formation of these olefins should be approximately the same for a syn E2 elimination.[6]

In order to examine the possibility of an α', β mechanism for the formation of both *cis*- and *trans*-cyclooctene, we prepared the *N*,*N*,*N*-dimethyl-*n*-butyl-*2*-d_1 iodides **5** and **6**. As anticipated, *trans*-cyclooctene from **5** was formed by a 100% syn mechanism. Elimination of the trans *2*-d_1 salt **6** showed the *cis*-olefin was also formed by a 100% syn pathway. More importantly, however, 100% (within experimental error) of the deuterium initially present in the starting salts **5** and **6** was found in the isolated olefins or the dimethylbutyl-

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[1] (a) J. Sicher, J. Zavada, and J. Krupicka, *Tetrahedron Lett.*, 1619 (1966); (b) J. Zavada, M. Svoboda, and J. Sicher, *ibid.*, 1627 (1966); (c) M. Pankova, J. Sicher, and J. Zavada, *Chem. Commun.*, 394 (1967); (d) J. Sicher and J. Zavada, *Collect. Czech. Chem. Commun.*, **32**, 2122 (1967).

[2] J. L. Coke and M. C. Mourning, *J. Amer. Chem. Soc.*, **90**, 5561 (1968).

[3] (a) G. Wittig and R. Polster, *Justus Liebigs Ann. Chem.*, **612**, 102 (1957); (b) G. Wittig and T. F. Burger, *ibid.*, **632**, 85 (1960); (c) J. Rabiant and G. Wittig, *Bull. Soc. Chim. Fr.*, 798 (1957).

[4] N. A. LeBel, *Advan. Alicyclic Chem.*, 195 (1971).

[5] (a) The starting materials were prepared according to the method of Coke.[2] The elimination reactions were carried out as described by Wittig[3] using potassium metal in liquid ammonia. The deuterium content of the starting materials and products was analyzed by mass spectrometry (11–14 eV). The mixture of *cis*- and *trans*-cyclooctene was separated by gas chromatography and each pure olefin was analyzed for deuterium. (b) Dimethylbenzylamine (21% d_1, 79% d_0) in NH_3 for 5 hr in the presence of KNH_2 lost 51% of its deuterium.

[6] The isotope effects for the formation of both *cis*- and *trans*-2-butene from 3-deuterio-2-bromobutane by an anti E_2 mechanism were found to be the same within experimental error: R. A. Bartsch, *J. Amer. Chem. Soc.*, **93**, 3683 (1971).