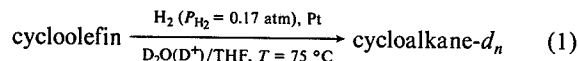# The Extent of Incorporation of Excess Deuterium in the Platinum-Catalyzed Reduction of Unsubstituted Cycloolefins by H_2 in D_2O/THF Increases with the Strain Energy of the Product Cycloalkanes[1]

T. Randall Lee and George M. Whitesides*

*Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138*

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This paper describes the isotopic compositions of cycloalkanes produced by the catalytic reduction of cycloolefins (C_nH_{2n-2}) using H_2 and platinum black in 1:1 v:v THF/$D_2O_{pD=1}$ (eq 1).[2] We

$$\text{cycloolefin} \xrightarrow[\text{$D_2O(D^+)$/THF, T = 75 °C}]{\text{H_2 (P_{H_2} = 0.17 atm), Pt}} \text{cycloalkane-}d_n \quad (1)$$

conducted the reductions under conditions in which the rate of mass transport of H_2 to the surface of the catalyst limited the rate of reaction.[3,4] Under these conditions, H_* on the surface equilibrates essentially completely with D_2O in solution. Figure 1 summarizes the isotopic compositions of the cycloalkanes.[5] The important observations are as follows: (1) the isotope of hydrogen found in the cycloalkanes was predominantly that present in D_2O rather than that present in H_2; (2) the cycloalkanes contained deuterium in large excess of that required for stoichiometric
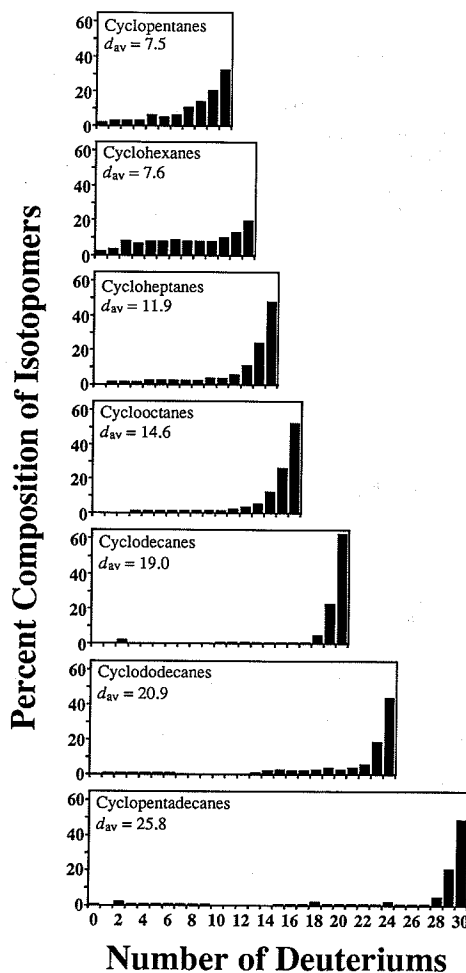

Figure 1. Isotopic distributions and values of d_{av} for the cycloalkanes from the reductions of the corresponding cycloolefins by H_2 and D_2O/THF (1:1 v:v; pD_{D_2O} = 1) over platinum black.[5] The difference in values of d_{av} from duplicate runs was, in all cases, ≤0.2.

(1) The National Science Foundation (Grant CHE-88-12709), the Office of Naval Research, and the Defense Advanced Research Projects Agency supported this work.

(2) We chose D_2O/THF (1:1 v:v; pD_{D_2O} = 1) because a survey of solvent systems indicated that this system yielded cyclooctanes having the highest content of deuterium in reductions of cyclooctene.

(3) We performed the reductions in a specially designed round-bottomed flask (volume = 225 mL): a small teat (volume ca. 10 mL) protruded from the bottom of the flask; a Swagelok valve and a rubber septum capped the flask. After charging the teat with a stir bar (3/8 × 3/16 in.) and 40 mg of Pt black, we purged the flask with Ar and added 0.5 mL of dry THF and 0.5 mL of D_2O (adjusted to pD = 1 with D_2SO_4). The apparatus was purged with a mixture of 10% H_2 in Ar for 1 min with stirring; the rate of rotation of the stir bar was 1400 rpm. We pressurized the vessel to 10 psi (P_{H_2} = 0.17 atm), stirred for 4 min, placed the flask in an oil bath (75 ± 3 °C), and stirred for 5 min. We removed the solvent via cannula and added the substrate (15–20 mg in 3 mL of D_2O/THF) via syringe. Stirring was started and continued for 1 h. Analysis by GC/MS indicated that all reductions were complete.

(4) Miller, T. M.; Izumi, A. N.; Shih, Y.-S.; Whitesides, G. M. *J. Am. Chem. Soc.* **1988**, *110*, 3146–3156.

(5) Isotopic compositions were determined by GC/MS.[6] The average content of deuterium, d_{av}, describes the extent of incorporation of deuterium. Isotopic abundances were corrected for natural abundance of ^{13}C. Values of d_{av} are probably accurate to ±0.3 D.

$$d_{av} = \sum_{n=1}^{m} n(\% \text{ alkane-}d_n)$$

(6) Miller, T. M.; McCarthy, T. J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1988**, *110*, 3156–3163.
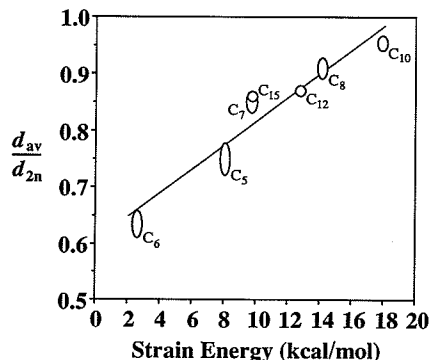
Figure 2. Values of d_{av}/d_{2n} vs strain energies of cycloalkanes (C_nH_{2n}).[5,17] For consistency, the strain energies are all calculated values, obtained using Macromodel V2.0.[18,19] The line drawn through the points was determined by linear regression.

reduction of the double bond (approaching complete exchange of D for H in some cases); and (3) each substrate gave the per-deuterated isotopomer as the major product.

The observation that extensively polydeuterated cycloalkanes can be produced from cycloolefins with H_2 as the reductant is remarkable and potentially useful in the synthesis of isotopically labeled compounds. The ability to incorporate deuterium into organic compounds by the metal-catalyzed reduction of olefins with H_2 and D_2O/THF avoids the need for D_2. In addition, this technique should be applicable to the incorporation of tritium into organic compounds.

Previous studies of the hydrogenation of olefins in protic solvents showed that surface alkyls on platinum rapidly undergo isotopic exchange of hydrogen with H* (D*) and that the product alkanes contain the isotope from the solvent (RO*H* or RO*D*).[7-13] Our results demonstrate that by working under mass-transport-limited conditions, isotopic exchange can be made more extensive than in these earlier reports. The exchange undoubtedly requires exchange between H* (D*) and the OH (OD) group of the solvent (eq 2). The mechanism of the exchange shown in eq 2 is not well established, although several mechanisms have been proposed.[10-16]

$$H* + ROD \rightleftarrows D* + ROH \qquad (2)$$

Because the exchange of H/D between the surface of platinum and the protic solvent is, under the conditions used here, faster than the conversion of surface alkyls to alkanes, the content of deuterium in the product alkanes provides a valuable mechanistic tool: a measure of the rate of exchange (and thus of C–H bond activation) of the surface alkyls relative to the rate of their reductive elimination as alkanes. Comparison of the ratio d_{av}/d_{2n} from the reduction of a series of cycloalkenes demonstrates the utility of this approach (Figure 2). These data indicate that the rates of C–H activation (relative to the rates of reductive elimination) of surface cycloalkyls decrease from cyclodecyl* to cyclohexyl*.

The value of d_{av}/d_{2n} correlates with the strain energy of the product cycloalkanes ($r = 0.95$).[17-19] Thus, as the cycloalkane is varied from one having low strain energy to one having high strain energy, the transition state for reductive elimination increases in energy relative to that for isotopic exchange. The two simple limiting hypotheses rationalizing this inference are that strain is *relieved* in the transition state for isotopic exchange (C–H activation) or that strain is *concentrated* in the transition state for reductive elimination.[21] We emphasize that $\Delta G^\ddagger$ for reductive elimination by reaction of R* with H_2 is dominated by the free energy term describing generation of H* by a mass-transport-limited process. We therefore hypothesize that the correlation in Figure 2 reflects primarily structure-dependent differences in rates of C–H activation.

The heterogeneous polydeuteration of hydrocarbons probably involves some combination of $\alpha\alpha$-activation, $\alpha\beta$-activation, and π-allyl formation.[22] The *differences* in strain energies between the transition states leading to these intermediates and the transition states leading to the cycloalkane products should correlate with d_{av}/d_{2n}. Calculating strain energies for the intermediates is, however, too complicated to be approached through realistic models of surface species.[23] To date, our efforts to obtain a correlation between the experimental values of d_{av}/d_{2n} and relative strain energies calculated for simple models of surface intermediates have not been successful.

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(16) Rolston, J. H.; Goodale, J. W. *Can. J. Chem.* **1972**, *50*, 1900–1906.

(17) The maximum possible content of deuterium in a cycloalkane is d_{2n}.

(18) We calculated strain energies for the lowest energy conformations of the cycloalkanes given in the following: Burkert, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph 177; American Chemical Society: Washington, DC 1982; pp 89–108 (for C_5–C_{12}). Anet, F. A. L.; Rawdah, T. N. *J. Am. Chem. Soc.* **1978**, *100*, 7810–7814 (for C_{15}). The strain energies for these conformations were calculated with Macromodel V2.0 using the MM2(85) parameter set: Still, W. C.; Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T. *MacroModel V2.0*; Dept. of Chemistry, Columbia University: New York, NY.

(19) The strain energies shown in Figure 2 were obtained by standard modification of the values given by force field calculations (SE = SE_{MM2} – $SE_{strainless}$).[20] The values for $SE_{strainless}$ were empirically determined to be $n \times 0.65$ kcal/mol for a given cycloalkane (C_nH_{2n}).

(20) See, for example: DeTar, D. F.; Tenpas, C. J. *J. Org. Chem.* **1976**, *41*, 2009–2013.

(21) There are several reports in the literature of correlations between the strain energy and the rates of reaction of functionalized cycloalkanes. For recent examples, see: Schneider, H. J.; Thomas, F. *J. Am. Chem. Soc.* **1980**, *102*, 1424–1425. Schneider, H. J.; Schmidt, G.; Thomas, F. *J. Am. Chem. Soc.* **1983**, *105*, 3556–3563.

(22) Lebrilla, C. B.; Maier, W. F. *J. Am. Chem. Soc.* **1986**, *108*, 1606–1616 and references therein.

(23) The hydrocarbon species believed to exist on the surfaces of noble metal catalysts were summarized recently: Cogen, J. M.; Maier, W. F. *J. Am. Chem. Soc.* **1986**, *108*, 7752–7762 and ref 22 of this paper.