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Deuterium and Carbon-13 Scrambling Processes in Isopropyl Cation*

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The degenerate rearrangement processes in *i*-propyl cation were studied using the isotopically double-labeled 2-propyl-2-¹³C₁-2-*d*₁ cation (A), which was obtained from the corresponding chloride using the molecular beam technique. The first step in the rearrangement is a shift of one of the methyl hydrogens to form *n*-propyl cation (or a species in its vicinity on the energy surface), followed by rotation of the methylene group. Rotation in one direction (Process I) leads to formation of isopropyl cation with an interchange of the methine proton with a methyl proton while rotation in the other direction (Process II) results in the formation of intermediate protonated cyclopropane. Through corner-to-corner proton shifts, the isotopes are completely scrambled before the reverse process returns the ion to isopropyl. Relative rates of Processes I and II were determined on the basis of the experimentally established composition of the mixture of isotopomers obtained in an early stage of scrambling, using Runge-Kutta integration to simulate the kinetics. It was found that Process I was faster ($k_I/k_{II} = 3.4$), meaning, according to the proposed mechanism, that hydrogen scrambles a little more rapidly than carbon.

INTRODUCTION

A great number of carbocations have been studied in stable solution. Of these, only the following are formally saturated secondary cations: isopropyl, *sec*-butyl, cyclobutyl, cyclopentyl, bicyclo[2.2.1]heptyl and bicyclo[2.1.1]hexyl cations. All except isopropyl and cyclopentyl have been shown to have non-classically bridged structures. Cyclopentyl, although there is experimental and theoretical evidence indicating that it is classical, has an extremely low barrier for degenerate hydride shifts and is therefore very close in energy to the non-classical, hydride-bridged transition state. Isopropyl is the only one of this group which has a classical structure not closely related to any bridged structure. Nevertheless, both hydrogens and carbons rapidly scramble in isopropyl cation. Using the NMR line-shape method, Saunders and Hagen¹ showed that the methyl

* Dedicated to Professor Dionis E. Sunko on the occasion of his seventieth birthday.

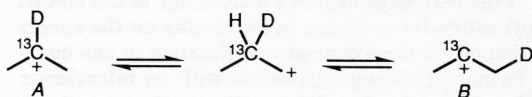
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and methine hydrogens are interchanging with a barrier of 16.4 kcal/mole (rate = 13.9 s^{-1} at 25°C). Labelling with ^{13}C surprisingly showed that carbons were also interchanging rapidly and at a similar rate.² This paper focuses on the mechanism for these exchanges through study of the relative rates of D and ^{13}C scrambling.

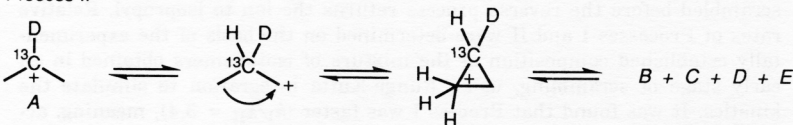
Since it would be very difficult to measure the rates of hydrogen and carbon scrambling separately precisely enough to get an accurate ratio, double labeled isopropyl cation³ was prepared to investigate the relative rates of these processes in a single experiment. We describe these results and consider how they may be interpreted mechanistically in view of other related experimental results and the theoretical calculations which have been reported over the last 20 years.⁴⁻⁷

When it was first studied,¹ proton scrambling in isopropyl was rationalized by proposing that a methyl hydrogen shifted to the center carbon to yield the *n*-propyl cation as an intermediate (Process I). If the hydrogen which was originally the methine proton moves to the methyl carbon, exchange occurs. In order to explain carbon scrambling, reversible closure of the *n*-propyl cation to protonated-cyclopropane (Process II) was considered. A further question which was asked was whether the protonated-cyclopropane could undergo corner-to-corner proton shifts before re-opening.^{1,8}

Process I



Process II



At the present time, our view of these processes must be altered as a result of additional experimental and theoretical results. The energies of both the corner- and edge- protonated-cyclopropanes are known to be far below the energy of the transition state for proton scrambling. Evidence for this is that *sec*-butyl cation interchanges inside and outside protons⁹ and carbons¹⁰ with barriers around 7.5 kcal/mole. This certainly proceeds *via* protonated-methylcyclopropane species (both corner- and edge-). High level calculations agree well with these results for *sec*-butyl and predict similar energies for corner- and edge-protonated cyclopropane itself.¹¹ We can thus confidently expect that, once closure to protonated-cyclopropane occurs, complete scrambling of the protons will occur before ring opening and return to isopropyl.

All *ab initio* quantum mechanical studies of carbocations demonstrate substantial structural effects which may be described as resulting from hyperconjugation. As described in elementary textbooks, hyperconjugation in carbocations involves no-bond resonance contributors which distribute the charge over hydrogens (and carbons for carbon hyperconjugation). It has been forcefully demonstrated recently that the calculated charges on atoms resulting from theoretical calculations are a strong function of where you draw the border between atoms.¹² However, predicted positions for the

nuclei are not in debate. Experimental and theoretical results usually agree quite well (with only small corrections for zero-point motional averaging). In all cases studied so far by high-level *ab initio* calculations, when a CH or CC bond is parallel to a carbocation p-orbital, that bond is lengthened compared with similar bonds not parallel to the p-orbital (bonds orthogonal to the p-orbital are shortened). Also, the angles which these bonds make with the bonds connected to the cation center are found to be substantially reduced (bonds orthogonal to the p-orbital have those angles increased). Experimentally, large secondary equilibrium and kinetic H/D isotope effects have been demonstrated to result from this hyperconjugation and also to be very strongly dependent on the dihedral angle the CH bond makes with the p-orbital.

For these reasons, we must be very conscious of which bonds are parallel to the p-orbital of carbocations. Representation of a bond to a carbocation center group as a single bond with free rotation is therefore misleading. Different dihedral angles between the p-orbital and the two CH and one CC bonds imply very different amounts of hyperconjugative interaction and geometric distortion. The energy of carbocations does not necessarily vary greatly with this rotation of the cationic group, since loss of the stabilization due to hyperconjugation with one group is usually compensated by gain in stabilization due to another group which can interact more favorably. The bending of the CH or CC bond toward the p-orbital which is a structural result of hyperconjugation is also the initial phase of a hydride or methide shift rearrangement.

RESULTS AND DISCUSSION

With the above considerations in mind, let us take a fresh look at the propyl cation. *Ab initio* calculations have not found any minimum resembling an *n*-propyl cation structure.⁵ Recent calculations at higher level give the same result.⁷ Therefore, it is probably incorrect to write the *n*-propyl cation as an intermediate. Nevertheless, both rearrangement processes must go through points on the energy surface in the vicinity of *n*-propyl. The structures of important points on the energy surface in this area will be a strong function of the dihedral angle on the CH₂⁺ group with respect to the CH and CC bonds of the isopropyl. An angle favoring CH hyperconjugation predisposes the ion to a hydride shift (downhill to isopropyl). An angle favoring CC hyperconjugation readies it for going downhill to corner-protonated cyclopropane and thus will result in complete scrambling of carbons and hydrogens.

Both rearrangement processes must begin with the shift of a hydride from a methyl to the center carbon. The energy goes up with this shift and we get to a structure of *n*-propyl geometry with the hydrogen which has shifted with its bond still parallel to the p-orbital on the CH₂. If the ion returns downhill to isopropyl at this point, no exchange of protons or carbons occurs and this process would produce no observable effect. In order to have any net interchange occur, the terminal methylene, containing the formal positive charge, must rotate. Turning it in one direction (arrow 1 on Figure 1) brings the other methylene hydrogen parallel to the cation p-orbital where it can hyperconjugate. When that hydrogen then migrates to the adjacent carbon reforming isopropyl cation, hydrogen exchange has occurred. The transition state for the exchange is the highest energy point on this rotation pathway. On the other hand, rotating the methylene group in the other direction (arrow 2 Figure 1) brings the methyl carbon to a hyperconjugating position. This structure can now go downhill to the corner-protonated-cyclopropane cation. Rapid scrambling of all of the hydrogens and carbons *via* the edge-protonated-cyclopropane would then be expected and statis-

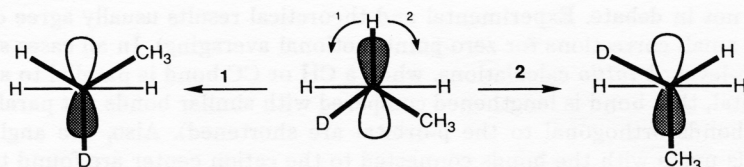
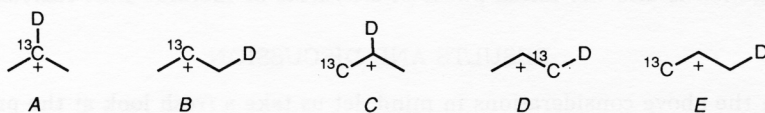


Figure 1

tical scrambling therefore results when this ion returns to isopropyl. Similarly, the transition state is that reached during rotation (arrow 2).

Starting with di-labeled isopropyl cation, the composition of the resulting mixture of different isotopomers obtained in the early stages of scrambling is a function of the relative rates of the processes resulting from rotating the methylene group in the two different directions. Starting with 2-propyl- d_1 - $2\text{-}^{13}\text{C}_1$ cation, four different double labeled isopropyl cation products (B, C, D, E) can be formed. Two isotopomers involve net migration of just one label: deuterium (B), and carbon (C), respectively, and two isotopomers involve moving both isotopes (D, E). Therefore, in order to establish the



products due to scrambling processes, the sample of double labeled isopropyl cation was warmed to -65°C during 15 minutes and then the spectrum was taken at much lower temperature in order to avoid further rearrangement. The composition of the mixture was:

$$31.2\% \text{ A} \quad 51.6\% \text{ B} \quad 17.2\% \text{ C, D and E}$$

Scrambling *via* the protonated-cyclopropane yields a probability of deuterium exchange of $6/7$ (There is a $1/7$ chance of finding the deuterium in the same position as it was in the starting material), and the chance of carbon exchange is $2/3$. The probability fractions for conversion to other isotopomers in Process II are therefore:

$$6/21 \text{ B} \quad 2/21 \text{ C} \quad 6/21 \text{ D} \quad 6/21 \text{ E}$$

The composition of the mixture therefore depends upon the ratio of the rates of Processes I and II (k_I/k_{II}). Thus, for each isotopomer, the formation rate was expressed according to the proposed mechanism, and a program using the Runge-Kutta integration method was used to evaluate the experimental results. For example, the rate of change of the concentration of isotopomer A can be expressed with the following equation:

$$dA/dt = 1/6 k_I[B] + 1/21 k_{II}([B]+[C]+[D]+[E]) - k_I[A] - 20/21 k_{II}[A]$$

For other isotopomers, the equations were written in a similar manner, and after applying the Runge-Kutta program, the computed areas on the NMR peaks were com-

pared with the experimental data until a satisfactory fit with the experimental data was obtained. The ratio of rate constants was obtained.

$$k_I/k_{II} = 3.4$$

Because of the way the experiment was carried out, we did not obtain highly accurate values for the individual rate constants for the two processes; since the time for thawing the sample was not negligible and some scrambling was occurring then.

The experimental results are in good agreement with the proposed mechanism, however the value of k_I/k_{II} is different from the previous results where it was found that the proton scrambling is just slightly faster than carbon scrambling (1.5 ± 0.5).⁸ The reason for the difference is that previously it was assumed that initial rates could be used while the Runge-Kutta integration has now permitted the complete kinetic model to be used. The detailed mechanism is also different from that used earlier as mentioned.

EXPERIMENTAL

Acetone-2-¹³C₁ was prepared from BaCO₃ (19.5 g, 0.099 mol) by liberating ¹³CO₂ with concentrated sulphuric acid, trapping the labeled carbon dioxide with methyl magnesium iodide (7.25 g magnesium and 43.0 g methyl iodide, both 0.31 mol), working up the Grignard to get the acetic acid-1-¹³C, neutralizing the acetic acid with LiOH, evaporating off the water and pyrolyzing the resulting lithium acetate-1-¹³C₁ (5.5 g, 0.082 mol) at 490–500 °C in overall yield of 2.3 g (40%).¹⁰

2-Chloro-propane-2-*d*₁-2-¹³C₁ was prepared from acetone-2-¹³C₁ which was reduced with lithium aluminum deuteride in dry ether by the standard procedure, and double-labeled parent alcohol, 2-propanol-2-*d*₁-2-¹³C₁ obtained (1.6 g, 0.026 mol) was converted into chloride with anhydrous ZnCl₂ (18.2 g) and 7.9 mL conc. hydrochloric acid. The yield of 2-chloro-propane-2-*d*₁-2-¹³C₁ was 0.7 g (33%).

Cation sample preparation

Cation samples were prepared by ionization of the 2-chloro-propane-2-*d*₁-2-¹³C₁ in the molecular beam apparatus as described previously.¹¹ Typically, antimony pentafluoride (0.3–0.4 mL) was codistilled with the precursor (0.05–0.08 mL) into an evacuated glass chamber cooled in liquid nitrogen. The solvent (1.5 mL total), sulfuryl chloride fluoride was distilled into the chamber before and after the codistillation of the precursor and superacid. The frozen mixture was then thawed slowly in a methanol-ethanol slush bath (~ -120 °C) and poured into attached NMR tubes in which the external capillaries (with acetone-*d*₆ in ether) were placed previously. The tubes were sealed and immediately frozen in liquid nitrogen.

NMR spectra

NMR spectra were recorded on a CFT-20 Varian 20 MHz NMR spectrometer. The temperature was measured with a pentane thermometer placed directly into the magnet. For the heteronuclear lock external acetone-*d*₆ was used, and peak positions were referenced to external ether. The spectrum used to calculate the product ratio was run in two modes. First, a 20° pulse was used and the proton decoupling frequency was turned off during the pulse delay (3 s) to allow the isomers, particularly A to relax (no proton on ¹³C atom) and to avoid NOE of peaks for isomers with protons on ¹³C (B, C, D, E). Then, in order to check whether some residual NOE was still taking place, spectrum was run with the proton decoupling off, and the ratio of 5 and 6 was compared. The results were essentially the same, 0.60 *vs.* 0.58. (The deviation is in the wrong direction to reflect possible residual NOE, but represents the uncertainty of the cut-and-weigh method used).

REFERENCES

1. M. Saunders and E. L. Hagen, *J. Amer. Chem. Soc.* **90** (1968) 6881.
2. G. A. Olah and A. M. White, *J. Amer. Chem. Soc.* **91** (1969) 5801.
3. A. P. Hewett, Ph.D. Thesis, Yale University, 1975.
4. (a) W. J. Hehre in *Applications of Electronic Structure Theory*; H. F. Schaefer, III, Ed., Plenum Press, New York, 1972. Chapter 7, p. 277; (b) L. Radom, D. Poppinger, and R. C. Haddon in *Carbonium Ions*; G. A. Olah, and P. v. R. Schleyer, Eds., Wiley, New York, 1976; Vol. V, Chapter 38, 002303.
5. K. Raghavachari, R. A. Whiteside, J. A. Pople, and P. v. R. Schleyer, *J. Amer. Chem. Soc.* **103** (1981) 5649.
6. M. J. S. Dewar, E. A. Healy, and J. M. Ruiz, *J. Chem. Soc., Chem. Commun.* (1087) 943.
7. W. Koch, B. Liu, and P. v. R. Schleyer, *J. Amer. Chem. Soc.* **111** (1989) 3479.
8. M. Saunders, P. Vogel, E. L. Hagen, and J. Rosenfeld, *Acc. Chem. Res.* **6** (1973) 53.
9. M. Saunders, E. L. Hagen, and J. Rosenfeld, *J. Amer. Chem. Soc.* **90** (1968) 6882.
10. G. E. Walker, Ph.D. Thesis, Yale University, 1983.
11. J. W. M. Carneriro and P. v. R. Schleyer, *J. Amer. Chem. Soc.* **112** (1990) 4064.
12. (a) C. L. Perrin, *J. Amer. Chem. Soc.* **113** (1991) 2865. (b) K. B. Wiberg and K. E. Laidig, *J. Amer. Chem. Soc.* **109** (1987) 5935. (c) K. B. Wiberg and K. E. Laidig, *ibid.* **110** (1988) 1872. (d) K. B. Wiberg and S. L. Schreiber, *J. Org. Chem.* **53** (1988) 783. (e) K. B. Wiberg, C. M. Breneman, and T. J. LePage, *J. Amer. Chem. Soc.* **112** (1990) 3379, 4177.
13. E. L. Hagen, Ph.D. Thesis, Yale University, 1969.

SAŽETAK

Procesi raspršenja deuterija i ugljika-13 u izopropil kationu

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Proučavani su procesi degeneriranog pregrađivanja, upotrebljavajući izotopom dvostruko obilježeni 2-propil-2- d_1 kation (A), dobiven iz odgovarajućeg klorida tehnikom molekuskog snopa. Prvi stupanj pregrađivanja obuhvaća premještaj jednog vodika s metilne skupine i stvaranje *n*-propil-kationa (ili vrste u njegovu bliskom susjedstvu na energijskoj plohi), nakon čega slijedi rotacija metilenske skupine. Rotacija u jednom smjeru (Proces I) vodi u nastajanje izopropil-kationa sa zamijenjenim vodicima na metilenskoj skupini, dok rotacija u drugom smjeru (Proces II) rezultira stvaranjem protoniranog ciklopropana kao međuprodukta. Premještanjem vodika s kuta na kut tročlanog prstena izotopi se potpuno raspršuju prije nego što otvaranjem prstena ponovno nastane izopropil-kation. Relativne konstante brzine Proces I i II određene su na osnovi eksperimentalno utvrđenog sastava smjese izotopomera dobivenoga u ranom stupnju raspršenja, upotrebljavajući metodu integracije Runge-Kutta za simuliranje kinetike. Nadeno je da je Proces I brži ($k_I/k_{II} = 3,4$), što u skladu s predloženim mehanizmom znači da se vodik raspršuje nešto malo brže od ugljika.