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Isotopic Scrambling in Di-^{13}C-labeled 2-Butyl Cation: Evidence for a Protonated Cyclopropane Intermediate

Gary E. Walker,[†] Olga Kronja,*[,‡] and Martin Saunders*[,†]

Department of Chemistry, Yale University, P.O. Box 208107, New Haven, Connecticut 06520-8107, and Faculty of Pharmacy and Biochemistry, University of Zagreb, A. Kovačića 1, 10000 Zagreb, Croatia

kronja@pharma.hr; ms@gaus90.chem.yale.edu

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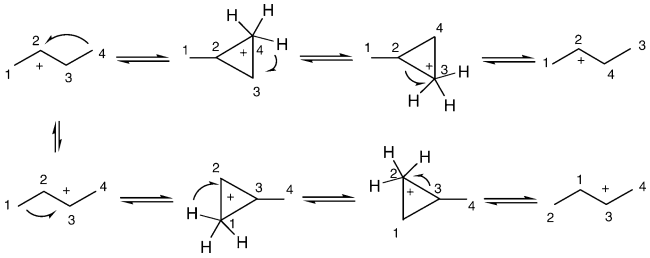
Abstract: The ^{13}C NMR spectrum of 2-butyl-1,2-$^{13}C_2$ cation (**1**) is unchanged on heating the sample to −78 °C, indicating no isomerization to another isotopomer. In contrast, the spectrum of 2-butyl-2,3-$^{13}C_2$ cation (**2**) shows rapid formation of all of the other isotopomers except **1**. These results are consistent with a protonated cyclopropane intermediate in the rearrangement process. In this mechanism, either C_1 and C_2 or C_3 and C_4 interchange. Only the bond between C_2 and C_3 breaks.

The ^{13}C NMR spectrum of the stable 2-butyl cation solution in antimony pentafluoride (SbF_5/SO_2ClF)[1] consists of two signals, with chemical shifts of 21.0 ppm for the outside carbons (C_1 and C_4), and 171.6 ppm for the inside carbons (C_2 and C_3).[2] Saunders and Kates have looked for broadening of these lines at low temperature and did not find any.[3] If it is assumed that the ion has the classical 2-butyl structure, the four different carbons would have to yield these two peaks through averaging by a very rapid, degenerate hydride shift. The free energy of activation for this hydride shift would have to be less than 2.4 kcal/mol.[3] This model is consistent with the proton spectrum, which gives two sharp peaks of area six and three for the averaged methyl protons and the averaged methylene and methine protons, respectively.

Another possibility to consider is that the ion has the static symmetrically hydrido bridged structure.[4] However, the proton spectrum of this ion would have two separate peaks for the bridging and nonbridging inside hydrogens. A bridged ion of this structure must be rapidly going to the classical ion as an intermediate in order to scramble the three inside hydrogens. In fact, there is no reasonable single structure that makes these three protons symmetrically equivalent. To account for the single peak for the inside protons, there **must** be an extremely rapid scrambling process with a low barrier.

SCHEME 1



Theoretical calculations indicate that the PES of the 2-butyl cation is extremely flat with two favorable minimum energy structures, the hydrido bridged structure and the classical structure stabilized with very strong hyperconjugation.[5]

Line broadening was observed at temperatures above −100 °C in the proton spectrum of the solution of 2-butyl cation, providing evidence that the inside and methyl protons are interchanging with a barrier of 7.5 kcal/mol.[6] A mechanism was proposed going through a protonated methylcyclopropane intermediate. This process would also interchange the inside and outside carbons. The mechanism via the protonated cyclopropane intermediate was examined theoretically, and the calculated barrier is essentially the same (8.5 kcal/mol) as that obtained for the methyl proton interchange by line shape analysis.[5]

The detailed mechanism through the proposed protonated cyclopropane mechanism is presented in Scheme 1. The first step involves the closure to a protonated methylcyclopropane intermediate followed by degenerate corner-to-corner proton shift and reopening of the ring. If this mechanism is correct, then C_1 and C_2 and C_3 and C_4, respectively, interchange positions in the rearranged cation, but only the C_2-C_3 bond breaks and the atoms that are C_1-C_2 and C_3-C_4, respectively, in the starting material remain attached to each other. The mechanism can be investigated by studying the rearrangement of isotopically labeled species.

We now report an experiment that strongly supports this protonated cyclopropane mechanism. Double-^{13}C-labeled cations were prepared as stable solutions ($SbF_5/SO_2ClF/SO_2F_2$): 2-butyl-1,2-$^{13}C_2$ cation (**1**) and 2-butyl-2,3-$^{13}C_2$ cation (**2**) from the corresponding bromobutanes. Details concerning the precursors and the corresponding cation preparations are given in the Experimental Section. It should be noted that the synthesis of 2-butyl-2,3-$^{13}C_2$ precursor resulted in the production of some precursor for the 2-butyl-1,2-$^{13}C_2$ cation (**1**), whereas the 2-butyl-1,2-$^{13}C_2$ precursor could be prepared without containing material that would give other isotopomers of the 2-butyl-1,2-$^{13}C_2$ cation (**1**) but only some monolabeled species due to the ^{13}C content of the starting $Ba^{13}CO_3$ (92%).

^{13}C NMR spectra of the samples **1** and **2** indicated drastically different behavior under given conditions. The

* To whom correspondence should be addressed. Tel: +385 1 48 17 108. Fax: +1 385 1 48 56 201.
[†] Yale University.
[‡] University of Zagreb.

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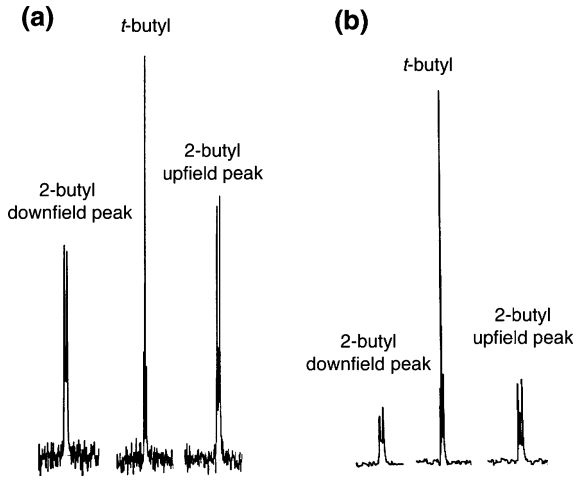
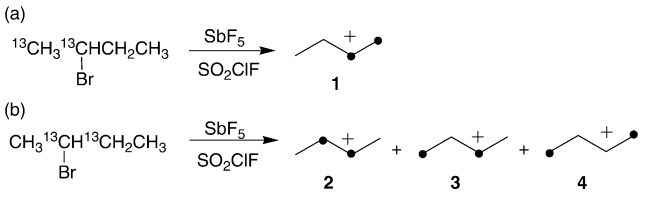


FIGURE 1. ^{13}C NMR spectrum of 2-butyl-[1,2-$^{13}C_2$] cation **1** (a) prior to and (b) after heating to −78 °C.

SCHEME 2



spectrum of **1** taken at −131 °C consists only of two doublets (J_{C1-C2} = 35.1 Hz) due to carbon−carbon spin coupling for the inside and outside carbons, and the small peaks located between the doublets due to the monolabeled 2-butyl cation (Figure 1a). The ratio between the peak areas of the dilabeled and monolabeled cations is 4.3 ± 1.7. To get evidence about whether other dilabeled isotopomers form, the sample was warmed at −78 °C for 30 min, which caused 80−90% of the ion to rearrange to the *tert*-butyl cation (Figure 1b).[1] Even after warming, the ratio of the areas of the doublet peaks that correspond to doubly labeled species and the peaks between the doublets remain the same (3.3 ± 0.7), indicating that the singlets between the doublet correspond only to the monolabeled cation and scrambling in the dilabeled species did not occur (Scheme 2a).

As mentioned above, the precursor for 2,3-dilabeled cation **2** contains a small amount of the precursor for the 1,2-dilabeled cation **1**. Therefore, if no scrambling occurred, the spectrum would have a large singlet in the downfield region (C_2 and C_3) due to cation **2** and two small doublets due to cation **1**. However, the spectrum taken at 125.76 MHz showed more signals (Figure 2a), indicating that scrambling of the label did occur. To make assignments more easily, the spectrum was recorded at both 125.76 and 67.89 MHz. The downfield parts of the spectra are compared in Figure 2.

There are four possible isotopomers of the doubly labeled 2-butyl cation (Scheme 2), and in the downfield peaks in the CMR spectrum signals of 1,2-, 1,3-, and 2,3-$^{13}C_2$ isotopomers (**1**, **2**, and **3**) could occur, since in the 1,4-$^{13}C_2$-labeled species (**4**) the "inside" carbons are only seen in natural abundance, and also the small amount of monolabeled cation. So, if complete scrambling occurs, the overall peak shape in the downfield region is determined by three components: a doublet that corresponds to **1** and the singlets that correspond to isotopomers **2** and **3**. For a similar reason, the upfield peaks of the scrambled mixture would have peaks for isotopomers **1**, **2**, and **4**.

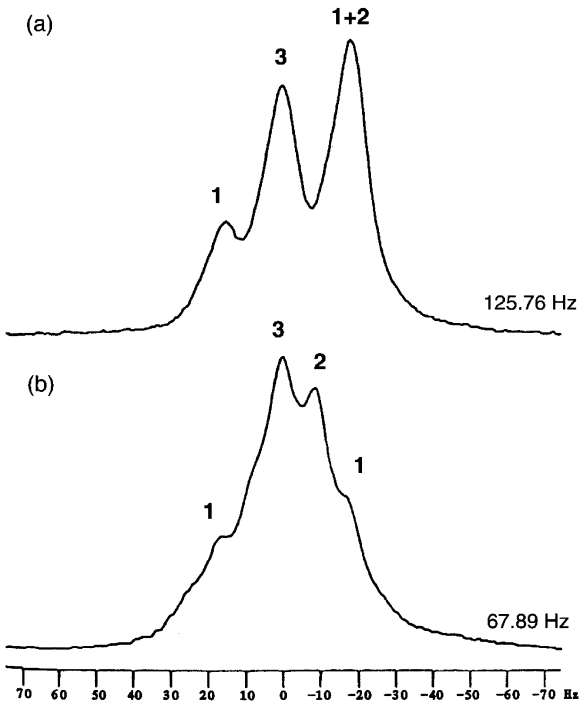


FIGURE 2. ^{13}C NMR spectrum of the downfield region of the mixture generated from 2-butyl-[2,3-$^{13}C_2$] cation **2** taken at (a) 125.75 and (b) 67.89 Hz.

Before interpreting the spectrum obtained, let us consider the relative position of the signals. The reason that it is possible to distinguish the signals is that there is a $^{12}C-^{13}C$ equilibrium isotope effect (EIE). Saunders, Kates, and Walker demonstrated that at equilibrium the positive charge slightly prefers to be located on the heavier isotope.[7] This preference perturbs the equilibrium and therefore shifts the position of the ^{13}C signal of the species with only one labeled carbon. However, **2** is a symmetrical structure and there is no EIE. Both chemical shifts of the downfield peaks of **1** (center of the doublet) and **3**, as well as a monolabeled compound, are expected to be slightly shifted downfield, since the fraction of structures in which the positive charge is on the ^{13}C is slightly larger than the fraction of structures in which the positive charge is on the ^{12}C. Consequently, the signal of the inside carbon of **3** (and the monolabeled cation) should be centered between the doublet that corresponds to **1**, whereas the peak for **2** is expected to be slightly shifted upfield. The magnitude of the shifts of the signal position caused by EIE should be temperature-dependent. Incidentally, if all of the ions had the symmetrical hydrido bridged structure, there would not be any EIE.

Even in static molecules, deuterium attached to or near a ^{13}C causes a small shift in the ^{13}C NMR position (the

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intrinsic isotope shift). We expect that a similar shift due to ^{13}C would be much smaller and can be neglected.

Comparing the spectra at different frequencies (Figure 2), it turned out that in the spectrum recorded at 125.76 MHz a peak that corresponds to the 2,3-^{13}C isotopomer (**2**) is shifted to overlap with the upfield peak of the 1,2-$^{13}C_2$ doublet (**1**), and the temperature-dependent central signal corresponds to the unsymmetrical labeled 1,3-$^{13}C_2$ isotopomer (**3**) and the monolabeled cation ($\Delta\delta = +0.144$ ppm at -143 °C and $+0.130$ ppm at -154 °C, relative to symmetrically labeled **2**)

Similarly, the large singlet centered inside the doublet in the upfield region of the spectrum correspond to unsymmetrical labeled cation **3** and symmetrically labeled **4,** as well as a little monolabeled species. These peaks cannot be distinguished because the β-EIE is too small to see.

It is important to mention that the fraction of cation **1** in the overall mixture is the same as the fraction of the precursor for cation **1** in the mixture of precursors, indicating that cation **1** is not formed during rearrangement of **2**. Therefore, we can conclude from the spectral data that cation **2** rearranges to all possible isotopomers except for **1**, whereas **1** does not go to the any of the others (Scheme 2).

In conclusion, the rearranged products of the doubly labeled species are completely consistent with the above proposed mechanism. According to this rearrangement, only cleavage of the C_2-C_3 bond occurs, interchanging the C_1 and C_2 (or C_3 and C_4) atoms only. Therefore cation **1** does not go to another isomer, since the two atoms that interchange are both labeled (or are both unlabeled). The observation that only **1** is not formed on rearrangement of cation **2** further supports the mechanism involving protonated cyclopropane, since to get that structure consecutive cleavage and reformation of the C_1-C_2 bond is necessary.

Experimental Section[8]

Cation Precursor Preparation. Acetylene-$^{13}C_2$. Magnesium powder (12.3 g, 0.506 mol) and $Ba^{13}CO_3$ (5.0 g, 0.025 mol) were intimately mixed, and the mixture was loaded into a quartz test tube. A 0.5 cm layer of magnesium powder was put on the top of the mixture. The tube was purged with argon, and then left under argon pressure. The bottom of the tube was heated strongly with a burner. After approximately 10 min, the reaction commenced, appearing as a red flame front that started at the bottom of the mixture. The tube was allowed to cool to room temperature.

The hydrolysis of the obtained barium carbide was carried out under a nitrogen atmosphere. Water was added slowly to the carbide, and the liberated acetylene was trapped in a U-tube, which was cooled in liquid nitrogen. Water was added until a vigorous reaction had subsided, and then the slurry was heated to boiling for 15 min. Then, the trap was closed off from the rest of the system, and the acetylene obtained was distilled into a gas storage bulb, degassed, and used for the next synthetic step. A yield of 10.6 mmol (84%) was determined: ^1H NMR (acetone-d_6) δ 2.33 ($^1J_{H-13C} = 248.9$ Hz, $^2J_{H-13C} = 49.1$ Hz, $J_{H-H} = 9.5$ Hz); ^{13}C NMR (acetone-d_6) δ 73.4.

1-Butyne-1,2-$^{13}C_2$. Into a round-bottom flask, equipped with Teflon-stopcock-protected syringe inlet port, a magnetic stirring bar, and a Teflon valve adapter was syringed 18.5 mL (0.059 mmol) of a 0.32 M solution of sodium dimsyl[9] in DMSO (2.14 M). The apparatus was connected to the vacuum line, the contents was frozen in liquid nitrogen and evaporated, and the solution was degassed. Acetylene-$^{13}C_2$ (5.9 mmol) was condensed into the manifold. When the pressure had built up sufficiently, the flask was opened to the manifold, and the absorption of acetylene was enhanced by vigorous stirring of the solution. On the end the reaction mixture was frozen in liquid nitrogen to condense the rest of the acetylene. The reaction mixture was allowed to stir for 1 h at the room temperature in the flask, which was closed off from the vacuum line.

The flask (connected with U-trap) was cooled in liquid nitrogen, and ethyl iodide (520 μL, 6.5 mmol) was dropped in from the syringe during a 50 min period in the atmosphere of dry nitrogen. After 5 h 0.5 mL ethylene glycol was injected and the system was evacuated. The DMSO solution was pumped off until bubbling stopped. The product obtained was separated from the residual DMSO and ethyl iodide by repeatedly cooling the liquid in an ice bath and allowing the volatile product to expand into the manifold, which was then condensed again. The final product was shown to be better than 99% pure by NMR, and the yield was 5.6 mmol (94%): ^1H NMR ($CDCl_3$) δ 2.33−2.14 (m, 2H) 1.93 (ddt, $^1J_{H-13C} = 247.0$ Hz, $^2J_{H-13C} = 49.12$ Hz, $^3J_{H-13C} = 6.6$ Hz, $^4J_{H-H} = 2.8$ Hz); ^{13}C NMR ($CDCl_3$) δ 72.22 (d), 53.75 (d, $^1J_{13C-13C} = 170$ Hz).

Propyne-$^{13}C_2$. The procedure was similar to that described above. Acetylene-$^{13}C_2$ (20.9 mmol), 10.1 mL of 2.14 M sodium dimsyl in DMSO, and 50 mL of extra DMSO were used. After connecting the flask with the sodium acetylide mixture to the U-trap line, 2.2 mL of dimethyl sulfate (23.2 mmol) was injected into it within a 2 min period, and the mixture was allowed to stir for 1.5 h. Propyne-1,2-$^{13}C_2$ was obtained with ca. 10% propyne-2,3-$^{13}C_2$ (20.8 mmol, 99%): ^1H NMR (acetone-d_6) δ 2.79−2.66 (weak), 2.49−2.46 (weak), 2.06−1.97 (moderate), 1.79−1.72 (strong), 1.58−1.49 (moderate); ^{13}C NMR (acetone-d_6) δ C-1 68.17, C2 (79.75, C-3 2.19 ($^1J_{13C-13C} = 172$ Hz, $^2J_{13C-13C} = 67$ Hz).

2-Butyne-$^{13}C_2$. The apparatus was the same as described for the preparation of propyne-$^{13}C_2$. Propyne-$^{13}C_2$ obtained in the pervious step was absorbed into the solution obtained from 12.2 mL of 2.14 M dimsyl in DMSO and 50 mL of extra DMSO. After connecting the system with U-trap line, 4 mL of dimethyl sulfate (0.042 mol) was added to the solution over period of 10 min. The solution was stirred for 3 h, and then 3 mL of ethylene glycol was injected. At the end of the preparation, it was found that the product was a mixture of propyne and 2-butyne. The mixture was separated by trap-to trap fractionation using the U-trap line. The first trap was cooled to -60 °C, and the second was cooled with liquid nitrogen. The yield of the sufficiently pure 2-butyne-$^{13}C_2$ was 11.6 mmol (56%), which was the mixture of 1,2-$^{13}C_2$ and 2,3-$^{13}C_2$ isotopomers: ^1H NMR (acetone-d_6) δ 21.70, 1.67, 1.63; ^{13}C NMR (acetone-d_6) δ C-1 2.44, C2 74.23 ($^1J_{13C1-13C2} = 69$ Hz).

2-Bromobutane-$^{13}C_2$ from 1-Butyne-1,2-$^{13}C_2$ (Precursor of Cation 1).[10] The three necked flask equipped with a Teflon-stopcock-protected syringe, reflux condenser, and a magnetic stirrer was connected to the vacuum line. A 7.0 mL portion of a 0.8 M solution of dibromoborane-dimethyl sulfide complex[11] in dichloromethane (0.56 mol) was injected into the flask. The content was frozen in liquid nitrogen, evaporated, and degassed, and then 0.056 mol of 1-butyne-1,2-$^{13}C_2$ was distilled in. The flask was closed off from the vacuum line, and the reaction mixture was allowed to stir overnight. The dichloromethane was then distilled off, and 5.0 mL of glacial acid was injected into the residue. The hydrogen that evolved was pumped off, and the mixture was allowed to stir overnight. It was then heated to 100 °C for 3 h. After cooling, the apparatus was opened and rinsed with 2 mL of dichloromethane and 2 mL of water, the layers were separated, and the aqueous layer was extracted with

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another 2 mL of dichloromethane. The dichloromethane solutions were combined and washed with 10% sodium hydroxide solution. The sodium hydroxide wash was back extracted with dichloromethane. The dichloromethane solution was concentrated by distillation on a helices-packed column. The residue was distilled to remove the nonvolatile matter. The pure 2-bromobutane was isolated by preparatory gas chromatography at 50 °C. The CMR spectrum indicated that the sample obtained was mostly 1,2-$^{13}C_2$ isotopomer with less than 10% of the 3,4-$^{13}C_2$ isotopomer: ^{1}H NMR (acetone-d_6) δ 4.17, 1.81, 1.67; ^{13}C NMR (acetone-d_6) δ C-2 54.09 ($^1J_{13C-13C}$ = 37 Hz), C-3 34.17 ($^1J_{13C}$ = 35 Hz), C-1 25.73 ($^1J_{13C-13C}$ = 37 Hz), C-4 11.75 ($^1J_{13C-13C}$ = 35 Hz).

2-Bromobutane-$^{13}C_2$ from 2-Butyne-$^{13}C_2$ (Precursor for Cation 2). The three-necked flask equipped with a Teflon-stopcock-protected syringe, reflux condenser, and a magnetic stirrer was connected to the vacuum line. A 6.4 mL portion of a 1.8 M solution of dibromoborane-dimethyl sulfide complex in dichloromethane (11.5 mmol) was injected into the flask and degassed, and then 11.6 mmol of 2-butyne-$^{13}C_2$ was condensed into the flask. The apparatus was attached to the end of the U-trap line, immersed in an ice bath, and stirred 10 min after it melted. Then it was immersed in an a 25 °C water bath stirred for 40 min, placed again in the ice bath, and quenched with 4 mL of propionic acid. The volatile material was pumped into the trap. The U-trap was cleaned and replaced, and the flask and the first U-trap were brought to atmospheric pressure with nitrogen. These were closed off together, and the trap was cooled with liquid nitrogen. The reaction mixture was kept between 90 and 110 °C during 2 h. After cooling, all volatile material was pumped into the trap and then distilled, yielding about 2 mL of liquid. Standing overnight, the product developed long needlelike crystals (not characterized). The remaining product was distilled into the tube containing ca. 0.5 g of powdered sodium hydroxide. After through mixing, the remaining liquid was distilled again. The pure product was isolated by preparatory gas chromatography on Porapack Q at 195 °C, and 0.3 mL of compound was obtained (see the preceding preparation for ^{1}H and ^{13}C NMR data).

Cation Sample Preparation. Cation samples were prepared by ionization of the corresponding halide in the molecular beam apparatus described previously in detail.[12]

For preparation of the samples with two ^{13}C labels, typically 0.5 g of antimony pentafluoride and 50 mg of butyl bromide were codistilled over a period of 0.5 h into the evacuated glass chamber cooled in liquid nitrogen. The solvent, which was a mixture of 2 mL of sulfuryl chloride fluoride and 3 mL of sulfuryl fluoride, was distilled into the chamber prior and following the codistillation. Then, the frozen mixture was thawed slowly in a methanol/ethanol slush bath (between −140 and −135 °C) and poured into the cooled attached NMR tubes in which external standard capillary (TMS in vinyl chloride) and external lock capillary (acetone-d_6 in vinyl chloride) was placed prior to attaching the NMR tubes. The tubes were sealed and immediately frozen in liquid nitrogen until used.

NMR Spectra. ^{13}C NMR spectra were recorded at 125.76 MHz at the given temperature. Cation samples were placed in a precooled NMR probe following temperature calibration with 2-chlorobutane.[13] Peak positions were referenced to external TMS in vinyl chloride, and external acetone-d_6 was used for the lock.

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