On the Mechanism of the Conversion of Methanol to 2,2,3-
Trimethylbutane (Triptane) over Zinc Iodide

John E. Bercaw, Paula L. Diaconescu, Robert H. Grubbs, Richard D. Kay,
Sarah Kitching, Jay A. Labinger, Xingwei Li, Parisa Mehrkhodavandi,
George E. Morris, Glenn J. Sunley and Patrick Vagner

Arnold and Mabel Beckman Laboratories of Chemical Synthesis, California Institute
of Technology, Pasadena, California, USA 91125; BP Chemicals Ltd, Hull Research
& Technology Centre, Kingston Upon Hull, North Humberside, HU1 28DS, England

jal@its.caltech.edu

Supporting Information

Table of Contents

NMR of triptane synthesized from \(^{12}\text{CH}_3\text{OH} + ^{13}\text{CH}_3\text{CH}_2\text{OH}\) S2
Analysis of NMR for carbene mechanism S5
Analysis of NMR for carbocation mechanism S6
NMR of triptane synthesized from $^{12}$CH$_3$OH + $^{13}$CH$_3$$^{13}$CH$_2$OH

A thick-walled glass tube was charged with 1.06 g ZnI$_2$, 0.21 g $^{12}$CH$_3$OH, and 0.064 g $^{13}$CH$_3$$^{13}$CH$_2$OH. The composition corresponds to a molar ratio of MeOH:EtOH = 4.7:1, and a total carbon isotope ratio of $^{13}$C:$^{12}$C = 30:70.

The tube was sealed under vacuum and heated in an oven at 200 °C, without agitation, for 4 h, and the organic layer extracted for examination by $^{13}$C NMR spectroscopy; a portion of the spectrum is shown in Figure S1. By comparison to the spectrum from an unlabeled reaction (see Figure 2, main text), it is clear that the signals for the internal carbons are considerably larger relative to those for the terminal methyls. Furthermore, each of the triptane signals consists of an apparent triplet — actually a singlet plus a doublet — showing that there is a significant probability (approximately 40%, from the relative intensities) that a $^{13}$C nucleus in any position has an adjacent $^{13}$C. The signals for C$_b$ and C$_c$ exhibit two additional outer peaks, corresponding to further overlap of a weak triplet signal arising from two adjacent $^{13}$C nuclei, implying that some label must get into methyl groups as well.
**Figure S1.** Part of $^{13}$C NMR spectra showing triptane signals for reaction of unlabeled MeOH with $^{13}$CH$_3^{13}$CH$_2$OH.

The intensities (as peak heights) of the various signals are shown in Table S1 — those for the weak outer peaks of the C$_b$ and C$_c$ signals are very approximate — along with the derived relative proportions of singlets and multiplets. The relative amount of $^{13}$C at each position is calculated from the peak heights and sensitivity factors, determined from the corresponding relative peak heights in a spectrum of unlabeled triptane, acquired under the same spectrometer conditions. The reliability of the latter values is probably no better than ± 25-50%, so the difference between C$_b$ and C$_c$ is not significant; the fact that the terminal positions (methyls and methylene) of triptene readily exchange (see main text) requires that the two internal positions have equal label occupancy. Even so, the relative enrichment in the internal vs. terminal positions is quite clear.
**Table S1.** NMR data for triptane from $^{12}$CH$_3$OH + $^{13}$CH$_3^{13}$CH$_2$OH

<table>
<thead>
<tr>
<th>Chemical shift (ppm)</th>
<th>$C_a$</th>
<th>$C_b$</th>
<th>$C_c$</th>
<th>$C_d$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27.8</td>
<td>33.4</td>
<td>38.4</td>
<td>18.5</td>
</tr>
<tr>
<td>Approximate splitting pattern</td>
<td>1:3:1</td>
<td>1:10:30:10:1</td>
<td>1:8:27:8:1</td>
<td>1:3:1</td>
</tr>
</tbody>
</table>

**Analysis of pattern**

- singlet: 59%
- doublet: 41%
- triplet: 14%
- singlet: 55%
- doublet: 39%
- triplet: 9%
- singlet: 56%
- doublet: 44%

<table>
<thead>
<tr>
<th>Total intensity (sum of peak heights)</th>
<th>103.5</th>
<th>26</th>
<th>91</th>
<th>68.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative $^{13}$C content</td>
<td>1.5</td>
<td>1.7</td>
<td>2.9</td>
<td>1 (defined)</td>
</tr>
<tr>
<td>Expected for statistical incorporation</td>
<td>1.5</td>
<td>0.5</td>
<td>0.5</td>
<td>1</td>
</tr>
</tbody>
</table>

We may analyze the splitting patterns with respect to the alternative proposed mechanisms. In both carbene- and carbocation-based routes, the reaction starts with ethanol-derived ethylene, which is cyclopropanated/ring-opened or methylated to give propene, and so on up to triptene, which is hydrogenated to triptane. As shown in the main text, the number of moles of triptane obtained can exceed the number of moles of promoter, so some of the triptane presumably arises from ethylene that comes from methanol. Assuming that label can get into the general pool by some route, we need to consider three modes of its incorporation into the product: in molecules that start with EtOH-derived ethylene; in molecules that do not start with EtOH-derived ethylene; and in the growth stage for both types. The last of these will primarily place label at terminal (methyl) positions, and the second will give statistical distribution among all positions, no
matter what the mechanism. However, the mechanism is crucial for the consequences of the first mode.

**Analysis of NMR for carbene mechanism**

Let us first examine, and dispose of, the carbene route. Cyclopropanation of ethylene would give a *symmetric* intermediate. As we continue along the route (shown in Scheme S1), when we reach the 2-methylbut-2-ene stage, we find that the amount of label in the terminal methyl positions is equal to or greater than the amount in the internal positions, depending on whether the C_4 olefin is but-2-ene or isobutene. From that point on to triptane the position of the labels is fixed. Since the other two modes of incorporating label will distribute it either statistically or (for carbons introduced at later growth stages) preferentially in methyl positions, this route is inconsistent with the observation that more label is found in the internal positions of triptane.
Analysis of NMR for carbocation mechanism

Now turn to our preferred, carbocation-based mechanism. Again, we first examine the fate of label from incorporation mode 1 (from EtOH-derived ethylene). Even though there is no symmetric intermediate, as in the prior case, the label will not all wind up in internal positions because propene should be readily protonated/deprotonated under the acidic reaction conditions, interconverting the two ends. Nor will the two $^{13}$C nuclei necessarily remain adjacent, as terminal positions of triptene were shown (main text) to exchange rapidly as well. (Similar exchanges probably take place at other stages of
growth as well, but that does not affect the final outcome.) The expected labeling pattern for triptane, neglecting for the moment any other mode of incorporation, is shown in Scheme S2.

**Scheme S2**

Straightforward statistical considerations predict the ratio of isotopomers shown, from which one can calculate the relative occupancies of positions a:b:c:d = 1.5 : 3.75 : 3.75 : 1, in qualitative agreement with observations (Table S1); the predicted occupancy of internal positions is somewhat too high, but perhaps not outside the range of precision of (corrected) measurements. However, the splitting patterns come out completely wrong: the internal signals should be mostly doublets (predicted singlet:doublet = 13:87 for b, 20:80 for c) which differ drastically from the observed values, which require no correction factor and hence should be quite reliable. Furthermore, this inconsistency
cannot be “fixed” by including the other modes of label incorporation. There must be a mechanism for reducing the fraction of adjacent doubly-labeled isotopologs, which requires exchanging some label out of EtOH-derived molecules.

The additional process we propose to account for the label distribution is reversible methylation during growth: a carbocation formed by methylation of an olefin can lose proton to give the next higher olefin, or it can lose a methyl group to revert to the lower olefin. This will have the consequence of scrambling labeled methyl groups (formed as shown in Scheme S2) with the ordinary MeOH-derived methyl groups. Scheme S3 illustrates this process at the C₄ stage. (In principle it could occur at any stage of growth, with different rates relative to growth; the experiments on methylation of 2,3-dimethylbut-2-ene with labeled MeOH and on isotope shifts in labeled triptene (see main text) suggest that exchange is not fast at the C₆ to C₇ stage, although it should be noted those experiments were carried out at lower temperatures.)

**Scheme S3**

The experiment involving reaction of $^{13}$CH₃OH and unlabeled i-PrOH (see main text) provides direct evidence that such a process does indeed operate. If so, isobutene derived from methylation of propene would retain the central $^{12}$C but exchange any terminal $^{12}$C
for $^{13}$C. In the $^{13}$C NMR spectrum of the gaseous products (condensed and redissolved) of that reaction, the signals for the olefinic carbons of isobutene are clearly distinguishable. That for the terminal carbon consists of a doublet ($^1J_{CC} \sim 71$ Hz) of triplets ($^2J_{CC} \sim 3$ Hz) along with a much weaker triplet in the middle, arising from the isotopologs $^{13}$CH$_2$=$^{13}$C(13CH$_3$)$_2$ and $^{13}$CH$_2$=$^{12}$C(13CH$_3$)$_2$ respectively; the relative total intensities are about 85:15. Thus in the latter isotopolog, which must have originated with (unlabeled) $^i$-PrOH, the terminal methyls are essentially completely exchanged for $^{13}$C. Because of facile proton exchange we would expect the methylene to be likewise completely labeled; in agreement, the signal for the central carbon is a doublet ($^1J_{CC} \sim 72$ Hz) of triplets ($^1J_{CC} \sim 41$ Hz).

Such a process will establish a quasi-equilibrated (“quasi” because we have no a priori way of knowing how fast the exchange process is compared to growth, although the above experiment suggests it is quite fast) pool of $^{12}$C- and $^{13}$C-methylating species, which will then participate in all subsequent steps — both methylation of intermediate olefins and synthesis of triptane directly from C$_1$ precursors. Hence the latter now must be included in the analysis as well.

We define $x$ as the fraction of $^{13}$C in the “methylating pool” that is established by these exchange processes (of course $x$ may vary over time, but we only observe the final, time-averaged outcome); and $y$ as the fraction of triptane molecules that originate from EtOH (as opposed to those arising entirely from MeOH). The initial propene population (before any methyl exchanges) will thus have the following isotopic composition:
We could now allow these three isotopologs to grow to triptane, with the constraint that, at the end, all methyl groups will have probability \( x \) of being labeled. We further have to allow for the fact that an internal position of a triptane molecule formed only from \( C_1 \) precursors also has \( x \) probability of being labeled. We include statistical factors, and for the first approximation, neglect any isotopologs arising from incorporation of more than one \(^{13}C\) from the methylating pool — i.e., we treat \( x^2 \) as negligibly small.

First, however, we must consider another question: do any di-labeled isotopologs survive (beyond those formed statistically, that is)? According to the postulated mechanism, the labeled methyl group in the middle isotopolog can exchange with the pool at all points along the growth process. But if the process occurs even at the \( C_3 \) stage, label will exchange out of the terminal (olefinic) position in the left-hand isotopomer, as shown in Scheme S4.

**Scheme S4**

![Scheme S4](image-url)
If that process is fast relative to growth, then the “founding population” will be, not the three isotopologs shown above, but just the following two:

\[
\begin{array}{c}
* \\
y \\
1-y
\end{array}
\]

The \(^{13}\text{CH}_3\text{OH/i-PrOH}\) experiment (see above) suggests that there is a fast exchange process at the \(C_3\) stage, as in Scheme S4, but it could also be explained by fast exchange at the \(C_4\) stage if Scheme S3 is modified to include interconversion between but-2-ene and isobutene. Let us first try to complete the analysis assuming that exchange at this level does not take place, and triptane grows up from all three of the isotopologs above. In that case, the predicted triptane labeling distribution is shown in Scheme S5, and the consequent predicted NMR peak patterns in Table S2.
Scheme S5

Table S2. Predicted NMR peak intensities from distribution in Scheme S4

<table>
<thead>
<tr>
<th></th>
<th>$C_a$</th>
<th>$C_b$</th>
<th>$C_c$</th>
<th>$C_d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singlet</td>
<td>$y(0.6x)/4 + (1-y)(3x/7)$</td>
<td>$y(1-x)/4 + y(0.4x)/4 + (1-y)(x/7)$</td>
<td>$y(1-x)/4 + y(0.4x)/4 + (1-y)(x/7)$</td>
<td>$y(0.4x)/4 + (1-y)(2x/7)$</td>
</tr>
<tr>
<td>Doublet</td>
<td>$y(0.6x)/2 + y(0.6x)/4$</td>
<td>$y(1-x)/2 + y(0.4x)/2 + y(0.6x)/4$</td>
<td>$y(1-x)/2 + y(0.6x)/2 + y(0.4x)/4$</td>
<td>$y(0.4x)/2 + y(0.4x)/4$</td>
</tr>
<tr>
<td>Triplet</td>
<td>—</td>
<td>$y(0.6x)/2$</td>
<td>$y(0.4x)/2$</td>
<td>—</td>
</tr>
</tbody>
</table>

This model cannot satisfactorily account for the observed patterns. The easiest way to see that is to note that the predicted singlet:doublet ratios for $C_a$ and $C_d$ are independent of $x$. For $C_a$, singlet:doublet $= 0.15y + 0.43(1-y) : 0.3y + 0.15y = 59:41$, from which we calculate $y = 0.46$; the analogous calculation for $C_d$ gives $y = 0.50$. But if we try to use a value for $y$ around 0.5 to calculate $x$ from similar equations for the singlet:doublet ratios...
for Cₐ and Cₖ, we get negative values. We can fit the singlet:doublet ratios for the internal carbons with much lower values of y; but then the methyl signals are predicted to be almost entirely singlets. It is not possible to get the singlet:doublet ratios close to the observed (~ 60:40) values for both internal and terminal positions simultaneously.

The alternative, then, must be the case: that only the central label in EtOH-derived propene survives. Then the predicted final triptane speciation (again neglecting double incorporation from the methylating pool for the time being; this is obviously not correct, as it predicts no triplet signal for the internal carbons, but we will deal with that later) is as shown in Scheme S6, and the intensity patterns in Table S3.

**Scheme S6**

\[
y(1-x)/2 + (1-y)x/7 \quad y(1-x)/2 + (1-y)x/7 \quad (1-y)(1-x)
\]

\[
y/2(3x/6) \quad y/2(3x/6) \quad (1-y)(3x/7)
\]

\[
y/2(2x/6) \quad y/2(2x/6) \quad (1-y)(2x/7)
\]

\[
y/2(2x/6)
\]
Table S3. Predicted NMR peak intensities from distribution in Scheme S6

<table>
<thead>
<tr>
<th></th>
<th>$C_a$</th>
<th>$C_b$</th>
<th>$C_c$</th>
<th>$C_d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singlet</td>
<td>$\frac{xy}{4} + \frac{(1-y)(3x)}{7}$</td>
<td>$\frac{y(1-x)}{2} + \frac{(1-y)x}{7} + \frac{xy}{6}$</td>
<td>$\frac{y(1-x)}{2} + \frac{(1-y)x}{7} + \frac{xy}{4}$</td>
<td>$\frac{xy}{6} + \frac{(1-y)(2x)}{7}$</td>
</tr>
<tr>
<td>Doublet</td>
<td>$\frac{xy}{4}$</td>
<td>$\frac{5xy}{12}$</td>
<td>$\frac{xy}{3}$</td>
<td>$\frac{xy}{6}$</td>
</tr>
</tbody>
</table>

In this case, if we solve for $y$ using the terminal intensity ratios as before, and then use that value to solve for $x$ using the internal ratios, a consistent solution can be found, with $y \sim 0.8$ and $x \sim 0.6$. We can now use those numbers to calculate the predicted intensities of all signals and compare to experimental results, as shown in Table S4. The agreement is quite good, certainly within the expected reliability of the data. Note that the intensities of the two internal peaks are predicted to be equal (as is obviously a requirement of the exchange steps in the mechanism); although the experimental (adjusted) values are not equal, the predicted value is very close to the average of the two.

Table S4. Comparison of experimental and predicted NMR data for approximate model

<table>
<thead>
<tr>
<th></th>
<th>$C_a$</th>
<th>$C_b$</th>
<th>$C_c$</th>
<th>$C_d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed singlet:doublet</td>
<td>59:41</td>
<td>54:46</td>
<td>60:40</td>
<td>56:44</td>
</tr>
<tr>
<td>Predicted singlet:doublet</td>
<td>59:41</td>
<td>56:44</td>
<td>65:35</td>
<td>59:41</td>
</tr>
<tr>
<td>Observed relative intensity</td>
<td>1.5</td>
<td>1.7</td>
<td>2.9</td>
<td>1 (defined)</td>
</tr>
<tr>
<td>Predicted relative intensity</td>
<td>1.5</td>
<td>2.4</td>
<td>2.4</td>
<td>1</td>
</tr>
</tbody>
</table>
However, this successful modeling can amount only to a qualitative validation of the mechanism, because the approximation of incorporating only a single label from the pool per molecule — treating $x^2$ terms as negligible — is obviously incompatible with the large value of $x$ obtained: there will be a large fraction of molecules with two or more such labels. (Those will account for the triplet components of the $C_{b,c}$ signals, of course.) The full statistical treatment cannot be solved analytically, as was the above approximation, but requires numerical fitting.

For simplicity let us assume that the mechanism described above is the only one for transferring label from EtOH into the general pool, and that the label introduced into internal positions from the general pool is small compared to that originating directly from EtOH. Since each EtOH-derived triptane molecule retains one labeled carbon and contributes the other to the pool, the probability of either internal position being labeled is $y/2$, and that for any one methyl position is $y/(7(1-y) + 6y)$.

Calculated patterns for $y = 0.6-1.0$ are shown and compared to experimental results in Table S5. The best agreement for the $C_a$ and $C_c$ signals is obtained for $y \approx 0.7$; for the $C_b$ and $C_c$ signals, $y \approx 0.9$. Values outside this range give markedly poorer matches for all signals. The relative total intensity at each position is only slightly dependent on $y$ in this model; the values are in reasonable agreement with observations, given the uncertainty of the latter as discussed earlier. Figure S2 shows the close match of observed and simulated splitting patterns for a value of $y = 0.8$, for the signals corresponding to $C_c$ and $C_d$. 
The fact that the $y$ value calculated in the previous approximate model falls right in the middle of the range that gives acceptable fits for this more realistic one suggests that the value $y$ will not depend strongly on the exact details chosen, and overall provides strong validation for the proposed mechanistic picture. It is likely that still better fits might be found by allowing $x$ and $y$ to vary independently, but the reliability/precision of the experimental data do not seem to warrant the (substantial) additional effort that would entail.

**Table S5.** Comparison of experimental and predicted NMR data for more realistic model.$^a$

<table>
<thead>
<tr>
<th></th>
<th>$C_a$</th>
<th>$C_b$</th>
<th>$C_c$</th>
<th>$C_d$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Observed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$y = 1.0$</td>
<td>59:41:1.5</td>
<td>46:39:14:1.7</td>
<td>55:36:9:2.9</td>
<td>56:44:1.0</td>
</tr>
<tr>
<td>$y = 0.9$</td>
<td>47:53:1.5</td>
<td>47:41:12:1.8</td>
<td>55:37:8:1.8</td>
<td>48:52:1.0</td>
</tr>
<tr>
<td>$y = 0.8$</td>
<td>52:48:1.5</td>
<td>50:40:10:1.8</td>
<td>58:35:7:1.8</td>
<td>51:49:1.0</td>
</tr>
<tr>
<td>$y = 0.7$</td>
<td>57:43:1.5</td>
<td>55:37:8:1.9</td>
<td>63:32:5:1.9</td>
<td>59:41:1.0</td>
</tr>
<tr>
<td>$y = 0.6$</td>
<td>64:36:1.5</td>
<td>62:32:6:2.0</td>
<td>68:28:4:2.0</td>
<td>62:38:1.0</td>
</tr>
</tbody>
</table>

$^a$ For each entry the top line shows relative intensity of singlet:doublet:triplet; the second line the total relative intensity with that of $C_d$ defined as 1.
Figure S2. Observed and simulated (y = 0.8) patterns for the $C_c$ and $C_d$ signals.