Effects of Geminal Methyl Groups on the Tunnelling Rates in the Ring Opening of Cyclopropylcarbinyl Radical at Cryogenic Temperature†,#

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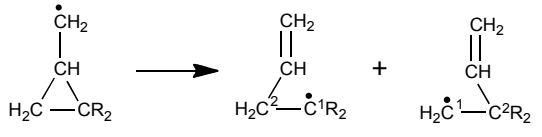
CVT + SCT calculations on the rate of tunnelling at 20 K in the ring opening of cyclopropylcarbinyl radical, substituted with geminal methyl groups at a ring carbon (1b), have been performed. The calculations predict that, contrary to expectations based on the effect of mass on the rate of tunnelling, the geminal methyl substituents in 1b should make the rate of ring opening to 1,1-dimethyl-3-butenyl radical (2b) 10^4 times faster than the rate of ring opening of unsubstituted cyclopropylcarbinyl radical (1a) to 3-butenyl radical (2a) and almost 10^6 times faster than the rate of ring opening of 1b to 2,2-dimethyl-3-butenyl radical (2c). The reasons for these unexpected findings are discussed.

The ring opening of cyclopropylcabinyl radical (**1a**) to 3-butenyl radical (**2a**), shown in Scheme 1, has been extensively investigated.[1] The extreme rapidity of this reaction has resulted in its widespread use as a "radical clock" for timing the rates of other free radical reactions.[2]

Professor Athel Beckwith made many important contributions to the study of this ring opening reaction,[3] including measuring the effects of substituents on it. For example, in 1989 Newcomb[4] and Beckwith[5] published back-to-back papers on the ring opening of 2,2-dimethylcyclopropylcarbinyl radical (**1b**). Although the tertiary radical center in **2b** makes it by far the thermodynamically preferred product, ring opening of **1b** to **2b** is only favored kinetically over ring opening to **2c** by a factor of about 6.5 at both 25°[4] and 60°.[5] The temperature dependence of the ratio of **2b**/**2c** is apparently small, and 1 kcal/mol probably is an upper limit on the difference between the E_a values for these two reactions. The results of several different types of *ab initio* calculations, performed by Schlegel and Newcomb,[6] also give values of slightly less than 1 kcal/mol for the difference between the barrier heights for ring opening of **1b** to **2b** and **2c**.

Scheme 1



1a, R = H
b, R = CH_3
c, R = D

2a, R = H
b, R = CH_3
d, R = D

2c, R = CH_3
e, R = D

The rate constants for the ring opening of the unsubstituted radical (**1a**) have been measured at temperatures as low as 128 K[7] and as high as 395 K.[8] An Arrhenius plot over this very wide temperature range is reasonably linear and gives E_a = 7.05 kcal/mol and log A = 13.15 s^{-1}.[9] The linear Arrhenius plot and the high A factor both suggest that, at least at the high end of this temperature range, the ring opening of **1a** to **2a** proceeds largely by passage over the reaction barrier, rather than by tunnelling through it.

We have been interested in the possibility that, at cryogenic temperatures, **1a** might undergo rapid ring opening by tunnelling, despite the fact that a CH_2 group, rather than a hydrogen atom, would have to tunnel in this reaction. Although not common, there are now several reactions in which experiments have shown that tunnelling by carbon can occur and occur rapidly.[10]

The two requirements for tunnelling by carbon to be rapid are a reaction barrier that is both low and narrow.[10] These requirements are met in the ring opening of **1a**. Indeed our previous calculations have predicted that, at temperatures up to 20 K, the ring opening of **1a** to **2a** should occur exclusively by temperature-independent tunnelling from the lowest vibrational level of **1a**, with $k = 2.22 \times 10^{-2}$ s^{-1}.[11]

Although the rate of ring opening of **1a** has not yet been measured at cryogenic temperatures, the intramolecular ^{13}C kinetic isotope effects (KIEs) on this reaction have been determined in solution between 173 – 253 K by Gonzalez-James and Singleton.[12] The KIEs that they measured support the hypothesis that tunnelling plays an increasingly important role in the ring opening of **1a** as the temperature is lowered. The experimental KIEs are fit much better by KIEs, computed with inclusion of small-curvature tunnelling (SCT) corrections, than by KIEs, computed without inclusion of tunnelling. In addition, an Arrhenius plot of the experimental $^{13}C/^{12}C$ KIEs is curved. The curvature provides purely experimental evidence, independent of comparisons between computed and measured rate constants, for a prominent role for tunnelling in the ring opening of **1a**.

In the ring opening of **1a**, ^{13}C tends to become concentrated at C2 of **2a**,[12] because C1 undergoes much more motion than C2 in the ring opening reaction; and the probability of tunnelling is higher for the lighter isotope of carbon (^{12}C). For the same reason, our SCT calculations predicted that, at 20 K, with geminal deuteria, attached to a ring carbon of **1c**, the deuteria will tend to wind up at C2 (as in **2e**), rather than at C1 (as in **2d**).[13] Therefore, it is easy to guess that the regiochemistry of the ring opening of **1b**, found around room temperature by Newcomb and Beckwith, will be reversed at 20K by tunnelling and that **2c**, not **2b**, will be the major product.

We have tested this prediction by carrying out tunnelling calculations on the ring opening of **1b** at 20 K. Our results show that this naive prediction is *completely wrong*. Our calculations on the ring opening of **1b,** by tunnelling from the lowest vibrational level, actually give a ratio of **2b**/**2c** that is computed to be many orders of magnitude larger at 20 K than the ratio of ca. 6.5, found by the experiments of Newcomb and Beckwith around room temperature.[4,5]

In carrying out tunnelling calculations on the ring opening of **1b**, we employed computational methodology similar to that we used in performing tunnelling calculations on the ring opening of **1a**.[11,12,13] Unrestricted electronic structure calculations were carried out with the B3LYP[14] functional and the 6-31+G(d,p) basis set.[15] Canonical variational transition state theory (CVT)[16] was used to locate the transition structure (TS) for the ring opening of **1** to **2**. Quantum effects on the reaction dynamics were computed semiclassically, using the small-curvature tunnelling (SCT) approximation.[17] The direct dynamics calculations were carried out with GAUSSRATE[18] as the interface between Gaussian 03[19]and POLYRATE.[20]

The UB3LYP/6-31+G(d,p) and the experimental activation energies for the ring opening of unsubstituted cyclopropylcarbinyl radical (**1a**) and the 2,2-dimethyl derivative **(1b**) are given in Table 1. The UB3LYP activation energies are in reasonable agreement with the experimental values, except that the calculated E_a for ring opening of **1b** to **2b** appears to be ca. 1 kcal/mol too low. Therefore, since the calculated difference in E_a values for formation of **2b** and **2c** is a little too high, the calculated product ratio of **2b** to **2c** of 25.4 at 300 K is about a factor of four larger than the observed value. [4,5]

Table 1. Enthalpy differences[a] at 300 K, computed by B3LYP/6-31+G(d,p) for the ring opening of cyclopropylcarbinyl radicals **1a** and **1b** and the E_a values that have been measured.

	1a → 2a	**1b → 2b**	**1b → 2c**
ΔH^{calc}	-3.4	-7.0	- 0.1
E_a^{calc}	7.3 [b]	5.0	6.7
E_a^{exp}	7.05[c]	6.1[d]	7.2[d]

[a]Values in kcal/mol. [b]7.6 kcal/mol with the 6-31G* basis set (ref. 11). [c]Ref. 9. [d]Ref. 6

The results of our CVT + SCT calculations, comparing the rates of ring opening of **1a** and **1b** at 20 K, are given in Table 2. Tunnelling rates are expected to decrease exponentially with the square root of the effective tunnelling mass.[21] Therefore, at first glance, it is not surprising that the geminal methyl groups in **1b** are computed to slow the rate of formation of ring-opened product **2c**, in Scheme 1 by a factor of 39.1, relative to the rate of formation of **2a** from **1a**.

Table 2. CVT+SCT rate ratios[a] calculated for ring opening of **1a-c** to **2a-e** at 20K.

Substituted C in product **2**	k (**1a**)/2k(**1b**)	k (**1a**)/2k(**1c**)
C^1	5.04 E-05	6.47[b]
C^2	39.1	0.85 [b]
Ratio C^1/C^2	7.76 E+05[c]	0.13[b,d]

[a] The calculated rates for ring opening of **1a** have been divided by 2, in order to eliminate the statistical factor that arises from the presence of two equivalent CH_2 groups in **1a**. [b]Ref. 13. [c]Predicted ratio of methyl groups at C^1 (**2b**) to methyl groups at C^2 (**2c**) in the ring opening of **1b**. [d]Predicted ratio of D_2 at C^1 (**2d**) to D_2 at C^2 (**2e**) in the ring opening of **1c**.

Also given in Table 2 are the H/D_2 KIEs that we previously calculated for the ring opening of **1c**.[13] It should be noted that the geminal deuteria in **1c** are not calculated to retard the rate of ring opening to **2e**; in fact, they are actually predicted to accelerate it by a factor of 1/0.85 = 1.2, relative to the rate of ring opening of **1a** to **2a**. Thus, the question arises, if geminal deuteria make the rate of ring opening of **1c** to **2e** slightly faster than the rate of ring opening of **1a** to **2a**, why do geminal methyl groups retard the rate of ring opening of **1b** to **2c** by a factor of 39.1, relative to the rate of ring opening of **1a** to **2a**?

Table 2 also shows that geminal deuteria are calculated to make the rate of ring opening of **1c** to **2d** a factor of 6.47 slower than the rate of ring opening of **1a** to **2a**. However, in stark contrast, the geminal methyl groups in **1b** are actually predicted to *accelerate* the rate of ring opening to **2b** by a factor of 1/(2 x 5.04 x 10^{-5}) ≈ 10,000.

The explanation of both of these unexpected predictions about the ring opening of **1b** to **2b** and **2c** must be that more than just the mass of the methyl groups affects the rate of tunnelling in the ring opening of **1b**. For example, as shown in Table 1 the geminal methyl groups make the calculated exothermicity of the ring opening of **1b** to **2b** larger than that of **1a** to **2a** by 3.6 kcal/mol. Probably as a direct result of this increased exothermicity, the methyl groups make the calculated barrier for **1b → 2b** 2.3 kcal/mol lower than that for **1a → 2a**. The methyl groups at C1 of **2b** obviously stabilize the radical center at this carbon; and, to a lesser extent, they stabilize the incipient radical center at this carbon in the transition structure for ring opening of **1b**.

The lower barrier to ring opening of **1b** to **2b**, compared to that for ring opening of **1a** to **2a**, makes tunnelling through the former barrier more probable than tunnelling through the latter.[21] Therefore, the effect of the methyl groups on reducing the barrier height for ring opening of **1b** to **2b** will, in contrast to the effect of the greater mass of the methyl groups, tend to increase the rate of tunnelling.

In addition, because the ring opening of **1b** to **2b** is more exothermic than the ring opening of **1a** to **2a**, according to Hammond's postulate,[22a] **1b → 2b** is likely to have an earlier transition structure than **1a → 2a**. An earlier transition structure for **1b → 2b** implies that this ring opening reaction should have a narrower barrier than **1a → 2a**.[22b] In fact, as shown in Figure 1, our POLYRATE calculations find that the barrier width in the ring opening of **1b** to **2b** is 0.54 Å, which is 21% smaller than the barrier width of 0.68 Å[23] in the ring opening of **1a** to **2a**.

The probability of tunnelling increases exponentially as the reaction barrier width and height are decreased.[21,24] Therefore, the 21% narrower barrier width and the 32% lower barrier height for **1b →2b** than for **1a → 2a** both tend to make ring opening of **1b** to **2b** much faster than the ring opening of **1a** to **2a**. According to the results in Table 2, the acceleration of the rate of tunnelling, due to the lower and thinner barrier for **1b → 2b** than for **1a →2a**, more than overcomes the larger effective tunnelling mass in the ring opening of **1b** to **2b**.

Do barrier height and/or barrier width also play a role in retarding the rate of tunnelling in the ring opening of **1b** to **2c**? As already noted, the geminal deuteria in **1c** are calculated actually to accelerate the rate of ring opening to **2e**;[13] so it is hard to see why the mass of the methyl groups should serve to retard the rate of ring opening of **1b** to **2c**. Moreover, as shown in Table 1, the barrier for ring opening of **1b** to **2c** is actually calculated to be 0.6 kcal/mol lower than that for ring opening of **1a** to **2a**. Therefore, a higher barrier cannot be the cause of the finding that **1b → 2c** is calculated to be 39.1 times slower than **1a → 2a**. Consequently, by process of elimination, the factor that is responsible for the slower rate of ring opening of **1b** to **2c**, relative to **1a → 2a**, must be a wider barrier for the former reaction.

As noted above, Hammond's postulate leads to the expectation that the less exothermic of two closely related reactions should have the wider barrier. [22b] As shown in Table 1, the ring opening of **1b** to **2c** is approximately thermoneutral; whereas, the ring opening of **1a** to **2a** is exothermic by 3.4 kcal/mol. Therefore, **1b → 2c** is likely to have a wider barrier than **1a → 2a**. In fact, as shown in Figure 1, our POLYRATE calculations find that the width of the barrier for ring opening of **1b** to **2c** is 0.83 Å, which

is 0.15 Å wider than the barrier in the ring opening of **1a** to **2a**.[24] The wider the barrier, the lower the rate of tunnelling; so the wider barrier to ring opening in **1b** → **2c** does, indeed, appear to be the reason that the geminal methyl groups retard the rate of this reaction, relative to the ring opening of **1a** → **2a**.

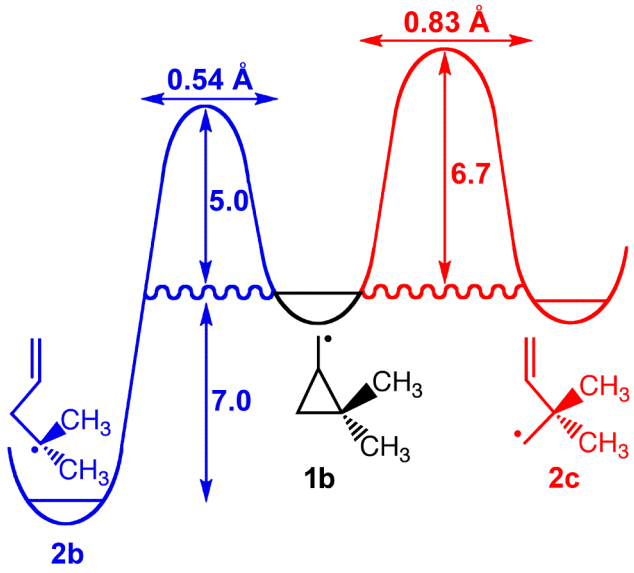


Figure 1. Schematic depiction of the B3LYP/6-31+G(d,p) enthalpy changes for ring opening of **1b** to **2b** and **2c** at 300 K. ΔH and E_a values are given in kcal/mol. The enthalpy difference between **2c** and **1b** is calculated to be $\Delta H = -0.1$ kcal/mol. The distances given are the calculated barrier widths, using the lengths of the scissile bonds as the reaction coordinates.

The combination of the calculated effects of the geminal methyl groups in **1b** on enhancing the rate of ring opening to **2b** and on retarding the rate of ring opening to **2c** leads to the prediction in Table 2 that, at 20 K, tunnelling will give a ratio of geminal methyl groups at C1 and C2 of **2b**/**2c** = 7.76 x 10^5. This ratio of the tunnelling rates for formation of these two products from **1b** at 20 K is 1.2 x 10^5 higher than the experimental ratio of **2b**/**2c** = 6.5 at temperatures between 300 and 360 K, where most of the ring opening reaction of **1b** occurs by passage over the reaction barrier, rather than tunnelling through it.

Table 1 shows that our B3LYP/6-31+G(d,p) calculations overestimate the difference between the barrier heights for formation of **2b** and **2c** from **1b**, but by less than 1 kcal/mol. Therefore, the calculated ratio of ≈ 10^6, favoring formation of **2b** over **2c** by tunnelling at 20 K, is large enough to lead us to be confident in making the following prediction: Experiments performed at 20 K would, in fact, find the ratio of **2b** to **2c** to be many orders of magnitude larger than the ratio of 6.5, measured at much higher temperatures by Newcomb[4] and by Beckwith.[5]

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Notes and references

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†Electronic Supplementary Information (ESI) available: [The optimized B3LYP/6-31+G(d,p) geometries, energies, thermal corrections, and harmonic frequencies for **1a**, **1b** and **2a**, **2b**, **2c** and the transition structures connecting them, and the CVT and CVT + SCT rate constants for these reactions. (10 pages)]. See DOI: 10.1039/b000000x/
#This Communication is dedicated to the memory of Professsor Athel Beckwith.

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