Comment on "Reactivity of Ketyl and Acetyl Radicals from Direct Solar Actinic Photolysis of Aqueous Pyruvic Acid"

Veronica Vaida,*,† Allison E. Reed Harris,† Rebecca J. Rapf,† Russell J. Perkins,† and Barry K. Carpenter‡

†Department of Chemistry and Biochemistry and Cooperative Institute for Research in Environmental Sciences, University of Colorado Boulder, Boulder, Colorado 80309, United States

‡School of Chemistry and the Physical Organic Chemistry Centre, Cardiff University, Cardiff CF10 3AT, United Kingdom

Over the past decade, a debate has emerged over the chemical mechanism to explain the aqueous photolysis of pyruvic acid and its photoproducts.[1−12] The first steps of the mechanism are generally agreed upon: pyruvic acid absorbs a photon, undergoes intersystem crossing and internal con-version, and then initiates further chemistry from the T_1 surface. From here, the mechanisms in the literature diverge. In 2006, Guzmán et al.[6] suggested a mechanism that proceeds by proton-coupled electron transfer to explain two products: dimethyltartaric acid and an oxo-C_7 species, for which two possible structures were provided. Griffith et al.[2] later presented a different mechanism, in which hydrogen abstraction by triplet-state pyruvic acid initiates radical chemistry that yields dimethyltartaric acid and other observed products,[2,8,9] including acetoin and lactic acid. Griffith et al.'s identification of acetoin and lactic acid was based on three independent NMR techniques: gHMBCad ($^{13}C-^{1}H$ correlation), ^{1}H gCOSY ($^{1}H-^{1}H$ correlation), and DOSY (viscosity corrected diffusion constant data).[2] The high level of agreement in the results from these techniques between standards and post-photolysis solutions offers irrefutable evidence that both acetoin and lactic acid are generated from the photolysis of aqueous pyruvic acid under certain conditions. Their identification was initially disputed by Eugene et al.;[3] however, Griffith et al.[4] addressed these concerns.

In their recent publication, Eugene and Guzmán[1] claim to have "unambiguously" identified their oxo-C_7 product, while again disputing the formation of acetoin and lactic acid,[2] making new arguments against these products on the basis of NMR and high-resolution mass spectrometry (HRMS) studies.[1] Because they do not observe signals with the mass-to-charge ratios that correspond to acetoin and lactic acid in their HRMS, they conclude the products are absent. However, as mass spectrometry is not inherently quantitative, lack of signal does not confirm a species' absence. Furthermore, work by Reed Harris et al.,[5] which builds from Griffith et al.'s mechanism,[2] indicates that, if sufficient oxygen is present during photolysis, the formation of acetoin and lactic acid is severely inhibited. Eugene and Guzmán[1] state that their solutions are usually sparged with air, so lack of acetoin or lactic acid under those conditions is, in fact, consistent with the Griffith et al. mechanism.[2] However, Eugene and Guzmán[1] also indicate some reactions were instead sparged with nitrogen, which would create conditions favorable for generating acetoin and lactic acid.[5] They do not specify the sparging conditions for each result presented in their recent paper, making it impossible to decipher which data correspond to which conditions. That is significant because of the well-documented sensitivity of pyruvic acid's photochemistry to oxygen.[5]

Beyond not accounting for some of the implications of previous work, problems persist in Eugene and Guzmán's recent paper. In the post-photolysis spectrum said to verify the absence of acetoin (Figure 6D),[1] they highlight four ^{1}H NMR peaks in regions where acetoin absorbs. While it is unclear what the expected product distribution should be because the sparging conditions were not specified, a standard addition of acetoin to this sample results in an increase in three of the four peaks, and Eugene and Guzmán cite the lack of increase in the peak at ~1.35 ppm as evidence that acetoin is absent.[1] It seems, however, more likely that the fourth peak results from another product, unrelated to acetoin; therefore, the increase in the three peaks upon addition of acetoin likely confirms its formation during the photolysis of pyruvic acid. Furthermore, the ^{1}H NMR spectral regions near 4.4 ppm, where quartets due to acetoin and lactic acid have been identified with numerous methods,[2] are not shown. Instead, they are assigned without further explanation to two products, namely, 2-hydroxy-2-((3-oxobutan-2-yl)oxy)-propanoic acid (one of the initially suggested oxo-C_7 structures[6]) and 2-(1-carboxy-1-hydroxye-thoxy)-2-methyl-3-oxobutanoic acid (termed oxo-C_8).[1]

Additionally, the mechanism proposed by Eugene et al.[1] is problematic for several reasons. First, the oxo-C_7 product is a hemiketal, a generally unstable class of compounds that exist in equilibrium with their carbonyl and hydroxyl components, here pyruvic acid and acetoin. Second, the suggested intermediate species, oxo-C_8, is a hemiketal of a tertiary alcohol. In general, tertiary alcohols almost never form hemiketals or hemiacetals.[14] This one would likely decompose into pyruvic acid and α-acetolactic acid, then thermally decarboxylate to form acetoin under ambient conditions. Third, radical reactions are generally indiscriminate, especially those that require escape from the initial solvent cage, as is required for this mechanism. It is odd, then, that reactions between the acetyl Y· radical (and its

hydrate) and other radicals in solution, reactions that would also generate α-acetolactic acid, have been neglected.[1]

The primary results from Eugene and Guzmán's recent publication are claims to have identified their proposed oxo-C_7 product and the corresponding oxo-C_8 intermediate.[1] There are, however, a number of issues stemming from their structural analysis of the oxo-C_7 product, which comes from a single ^{13}C gCOSY experiment. A modified version of Eugene and Guzmán's Figure 4[1] depicting these data is included here (Figure 1) with several lines overlaid for clarity. The most

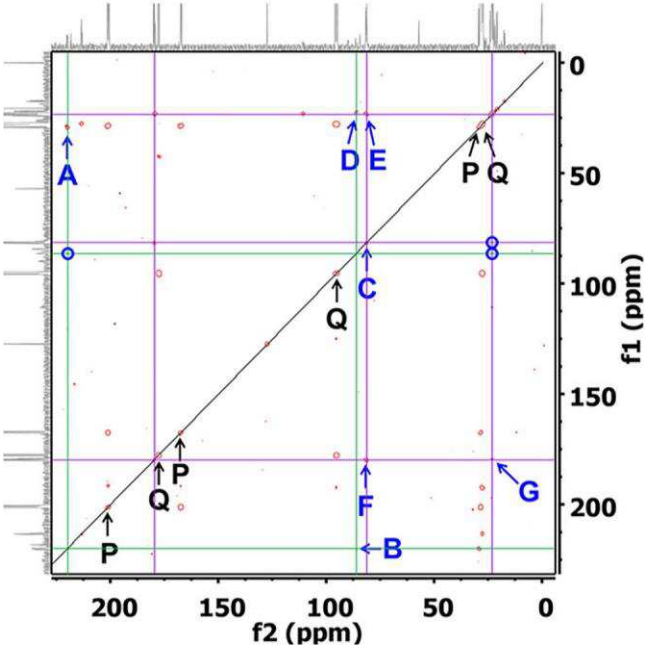

Figure 1. 150 MHz ^{13}C gCOSY NMR spectrum from Eugene and Guzmán,[1] with lines added for clarity. The black line is drawn through on-diagonal peaks, which correspond to the one-dimensional ^{13}C spectrum. The green lines connect the cross peaks originally labeled A, B, and D, while the purple lines connect the cross peaks originally labeled E, F, and G. Circled regions indicate where the cross peaks B, D, and E are absent from one side of the diagonal.

obvious issue is their interpretation of "cross peak C" as a structural link between the carbon signals at ~81 and ~86 ppm. The peak at ~81 ppm, however, is an on-diagonal peak, and, therefore, cannot be indicative of couplings between any carbons. This "connection" is the only evidence that all of the peaks assigned to the oxo-C_7 species exist on the same molecule. Instead, without "cross peak C", it is likely that the sets of cross peaks A, B, and D, and E, F, and G come from two different molecules. Furthermore, their corresponding shifts and implied couplings are consistent with acetoin and lactic acid. Finally, gCOSY spectra should be totally symmetric about the diagonal, indicating peaks that do not appear on both sides have low intensities, near the cutoff threshold, and, therefore, may be due to noise instead of couplings. Cross peaks B, D, and E are very weak, each appearing on only one side of the diagonal (see blue circled regions in Figure 1), making their identification as cross peaks speculative.

Because of this problematic two-dimensional identification of the oxo-C_7 product, the remaining structural information provided for oxo-C_7 relies on experimentally unverified one-dimensional ^1H NMR assignments that are based solely on predictive software, which may not account for deviations in chemical shift that occur in mixed solutions. This is also true for the oxo-C_8 product, as no two-dimensional evidence for the structure is presented. Their other attempts at identification of the compounds, mass spectrometry and carbonyl labeling chemistry, only confirm that the observed products have chemical formulas of $C_7H_{12}O_5$ and $C_8H_{12}O_7$ and contain one and two carboxylic acid groups, respectively, as well as one additional carbonyl group each. This does not provide structural evidence about the linkages between functional groups, and, therefore, no direct structural evidence for the oxo-C_8 product is presented.[1]

To conclude, despite the claims of Eugene and Guzmán,[1] they do not structurally identify their oxo-C_7 and oxo-C_8 products, thereby failing to confirm their mechanism. Their recent paper also does not disprove the generation of lactic acid and acetoin under oxygen-limited conditions. Furthermore, the mechanism of Griffith et al.,[2] with expansions by Reed Harris et al.[5] and Rapf et al., [12] is entirely consistent with the data presented by Eugene and Guzmán.[1]

AUTHOR INFORMATION

Corresponding Author

*E-mail: Vaida@colorado.edu.

ORCID

Veronica Vaida: 0000-0001-5863-8056

Allison E. Reed Harris: 0000-0002-1731-1687

Russell J. Perkins: 0000-0002-2351-2362

Notes

The authors declare no competing financial interest.

REFERENCES

(1) Eugene, A. J.; Guzman, M. I. Reactivity of ketyl and acetyl radicals from direct solar actinic photolysis of aqueous pyruvic acid. J. Phys. Chem. A 2017, 121, 2924−2935.

(2) Griffith, E. C.; Carpenter, B. K.; Shoemaker, R. K.; Vaida, V. Photochemistry of aqueous pyruvic acid. Proc. Natl. Acad. Sci. U. S. A. 2013, 110, 11714−11719.

(3) Eugene, A. J.; Xia, S.-S.; Guzman, M. I. Negative production of acetoin in the photochemistry of aqueous pyruvic acid. Proc. Natl. Acad. Sci. U. S. A. 2013, 110, E4274−E4275.

(4) Griffith, E. C.; Carpenter, B. K.; Shoemaker, R. K.; Vaida, V. Reply to Eugene et al.: Photochemistry of aqueous pyruvic acid. Proc. Natl. Acad. Sci. U. S. A. 2013, 110, E4276−E4276.

(5) Reed Harris, A. E.; Ervens, B.; Shoemaker, R. K.; Kroll, J. A.; Rapf, R. J.; Griffith, E. C.; Monod, A.; Vaida, V. Photochemical kinetics of pyruvic acid in aqueous solution. J. Phys. Chem. A 2014, 118, 8505− 8516.

(6) Guzman, M. I.; Colussi, A. J.; Hoffmann, M. R. Photoinduced oligomerization of aqueous pyruvic acid. J. Phys. Chem. A 2006, 110, 3619−3626.

(7) Closs, G. L.; Miller, R. J. Photo-reduction and photo-decarboxylation of pyruvic acid - applications of CIDNP to mechanistic photochemistry. J. Am. Chem. Soc. 1978, 100, 3483−3494.

(8) Leermakers, P. A.; Vesley, G. F. Photolysis of pyruvic acid in solution. J. Org. Chem. 1963, 28, 1160−1161.

(9) Leermakers, P. A.; Vesley, G. F. Photochemistry of alpha-keto acids and alpha-keto esters. 1. Photolysis of pyruvic acid and benzoylformic acid. J. Am. Chem. Soc. 1963, 85, 3776−3779.

(10) Davidson, R. S.; Goodwin, D.; De Violet, P. F. The mechanism of the photo-induced decarboxylation of pyruvic acid in solution. Chem. Phys. Lett. 1981, 78, 471−474.

(11) Davidson, R. S.; Goodwin, D. The role of electron transfer processes in the photoinduced decarboxylation reaction of α-oxo-carboxylic acids. J. Chem. Soc., Perkin Trans. 2 1982, 1559−1564.

(12) Rapf, R. J.; Perkins, R. J.; Carpenter, B. K.; Vaida, V. Mechanistic description of photochemical oligomer formation from aqueous pyruvic acid. J. Phys. Chem. A 2017, 121, 4272−4282.
(13) Perkins, R. J.; Shoemaker, R. K.; Carpenter, B. K.; Vaida, V. Chemical equilibria and kinetics in aqueous solutions of zymonic acid. J. Phys. Chem. A 2016, 120, 10096−10107.
(14) McKenna, F.; Tartar, H.; Lingafelter, E. Studies of hemiacetal formation in alcohol-aldehyde systems. II. Refraction studies. J. Am. Chem. Soc. 1953, 75, 604−607.