Air–water interface effects on the regioselectivity of singlet oxygenations of a trisubstituted alkene

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ABSTRACT

The regioselective synthesis of allylic hydroperoxide sulfonates by singlet oxygenation at the air–water interface has been found to depend on the concentration of the alkene sulfonate and added calcium salt. The regioselectivity is proposed to originate from an orthogonal alkene relative to the water surface for preferential methyl hydrogen abstraction by airborne singlet oxygen in an ene reaction. The findings hint that the air–water interface is a locale for synthetic reactions.

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Introduction

Organic chemists have yet to exploit the air–liquid interface for synthetic reactions. Nature—on the other hand—has synthesized complex molecules with prebiotic chemistry at the air–water interface[1] or in appropriate dynamical micellar systems.[2] Indeed, reactions at phase boundaries (e.g., air–water,[3] liquid–liquid,[4] solid surfaces[5]) can be unique and provide selectivity relative to the bulk phase. Such selectivity was recently seen at the air–water interface by airborne $^1O_2$ with a trisubstituted alkene surfactant, 8-methyl-non-7-ene-1 sulfonate (**1**) (Fig. 1).[6,7] Two hydroperoxides were formed in an ene reaction,[6] one was a secondary hydroperoxy sulfonate (**2**) and the other was a tertiary hydroperoxy sulfonate (**3**) with the preferred formation of regioisomer **2**. In contrast, the homogeneous $^1O_2$ ene reaction with trisubstituted alkenes such as 2-methyl-2-pentene occurs without selectivity for methyl and methylene hydrogens,[8] producing secondary and tertiary hydroperoxides in a ~1:1 ratio. Scheme 1 shows an exception[9] where a sterically hindered allylic group leads to methylene H abstraction and preference for the tertiary regioisomer due to an unfavorable 1,3-interaction of the proximal perepoxide oxygen with the large allylic group.

The purpose of this Letter is to extend our study on the regioselectivity of airborne $^1O_2$ with **1**, which we now report depends on reagent concentration and added calcium salt. Hydroperoxides **2**

and **3** are the only products with percent conversions reaching as high as 100%, where lower alkene **1** concentrations increased the regioselectivity for **2**, but concentrations above the critical micelle concentration (CMC), or with the addition of Ca^{2+} ions or use of acetonitrile–water mixtures showed no regioselective preference for **2** over **3**.

Results and discussion

Figure 1 shows our device, which resembles a flow system[10] and a device developed by Midden[11] for the clean and pure production of $^1O_2$. Our device irradiated samples from above with red diode light through a silica wafer. The silica wafer had a green color as it was coated with aluminum(III) phthalocyanine (Pc) chloride tetrasulfonic acid. Pc sensitizers often are not maintained as monomers in H_2O,[12] which was not of concern for us because the sensitizer wafer was not in contact with water. In Figure 1, $^1O_2$ gas was formed at the bottom of the wafer, and crossed an air gap to reach **1** at the water layer underneath.

Included in Table 1 are data for four reaction conditions that indicate the importance of environmental factors in the alkene sulfonate **1** photoperoxidation: (i) with a concentration of **1** (1 mM) that covered the water with a single layer of alkene molecules, a 7:3 regioselective preference for hydroperoxide **2** over **3** was seen (Table 1, entries 1 and 2). However, the selectivity of hydroperoxide products (**2** and **3**) was lost, (ii) with a 25-mM concentration of **1** (i.e., above its CMC, 9.7 mM)[6] (entries 2 and 3), (iii) with added Ca^{2+} ions ($CaCl_2$, 1–10 mM) (entries 4–6), and (iv) in an

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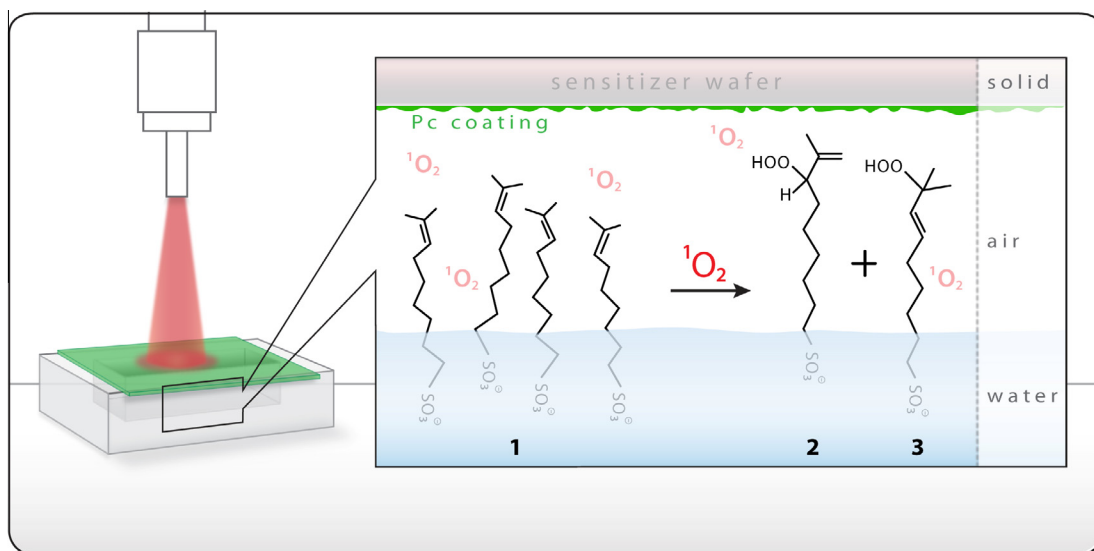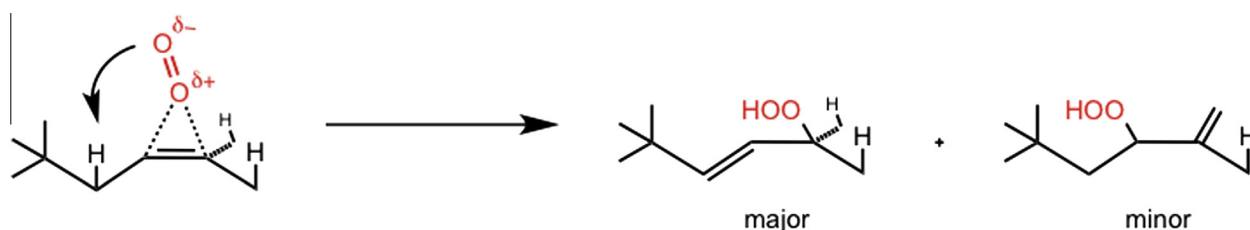 E-mail address: agreer@brooklyn.cuny.edu (A. Greer).

Figure 1. Schematic of the three-phase reaction for the delivery of airborne $^1O_2$ to the water surface. Red laser light passes through a sensitizer-bound glass wafer which is not in contact with the water. A small air space between the wafer and solution is bridged before $^1O_2$ gas reaches the liquid for alkene oxidation.

Scheme 1.

Table 1
Yields and ratios of hydroperoxides **2** and **3** formed by air–liquid $^1O_2$-ene reaction[a]

Entry	Interface	[1] (mM)	CaCl₂ added (mM)	% Yield[b]	Product ratio 2:3[b,c]
1	Air–H₂O	1	0	54 ± 4	70:30 (±5)
2	Air–D₂O	1	0	92 ± 2	69:31 (±1)
3	Air–D₂O	25	0	25 ± 6	47:53 (±2)
4	Air–D₂O	1	1	25 ± 7	52:48 (±2)
5	Air–D₂O	1	5	20 ± 7	49:51 (±1)
6	Air–D₂O	1	10	20 ± 8	41:59 (±5)
7	Air–liquid [CH₃CN/ H₂O (9:1)]	1	0	46 ± 4	43:57 (±3)
8	Air–liquid [CD₃CN/ D₂O (9:1)]	1	0	100 ± 1	49:51 (±1)

[a] Samples (0.6 mL) were illuminated with 669-nm diode laser light exiting a fiber optic positioned above the sensitizer wafer for 1 h at 26 °C. Airborne $^1O_2$ was produced at the sensitizer wafer and crosses an air gap to reach the solution. The distance between the wafer and the liquid surface in water was ~0.4 mm (at the walls of the vessel) to 1.5 mm (center of meniscus), and was ~1 mm for the acetonitrile–water samples.

[b] The values shown here are an average of 2 or more measurements.

[c] The ratio of **2** and **3** was calculated from the integration of ^1H NMR signals at 4.8 and 5.5 ppm, respectively.

acetonitrile/water mixture to dissolve **1** (entries 7 and 8). The efficiencies of the reaction by airborne $^1O_2$ transfer to solution were also investigated.

Singlet oxygen reactions are usually very sensitive to solvent isotope effects;[13] for example, in homogeneous solution the $^1O_2$ lifetime ($\tau\Delta$) is 20-fold lower in H₂O (3.5 µs) compared to D₂O (65 µs). We found an interesting contrast that the product yields from our $^1O_2$ reaction on a protio surface are only 2-fold lower than

on a deutero surface (compare entries 1 with 2, and 7 with 8). This modest solvent isotope effect in quenching of $^1O_2$ by **1** is rationalized by $^1O_2$ not transferring deep into the solution. It may penetrate into the solution distances of 880 nm in D₂O and in 150 nm in H₂O,[14] where the surroundings and location of the hydrophobic group of **1** play a role in its reactivity.

Based on our findings, the orientation of the alkene is proposed to be important (Fig. 2). In Figure 2i, the regioselectivity at sub-micellar concentrations is proposed to arise from a perepoxide transition state (TS) oriented with methyl groups pointed up in a less solvated state for easier abstraction by airborne $^1O_2$. With an orthogonal sheet surfactant, the hexyl sulfonate chain in **1** is not acting as a bulky allylic group as mentioned in the Introduction, or else **3** and not **2** would be the anticipated major product.[9] A product dependence on alkene wetting would connect to an ongoing discussion in $^1O_2$-ene chemistry, the idea of the perepoxide as a transition state versus an intermediate in gas and solution phases,[15–17] which has been of substantial interest. In Figure 2ii–iv, the methyl and methylene hydrogens appear to be equally abstractable in **1** and the regioselectivity is lost. In Figure 2ii, above the CMC, $^1O_2$ can oxidize but also proceed through the surfactant monolayer and reach the micelle, where micelles can assist in O₂ solubilization compared to that in the surrounding aqueous solution[18] and $^1O_2$ likely collides with several micelles during its lifetime.[19] In Figure 2iii, the Ca²⁺ additive induces an accumulation of **1** at the air–water interface due to its suspending power. Thus, the orthogonal geometry is thought not to be preserved in the presence of Ca²⁺ ions. In Figure 2iv, the lack of selectivity in acetonitrile/water can be explained where the surfactant is solubilized and not expected to adsorb at the interface or aggregate well for
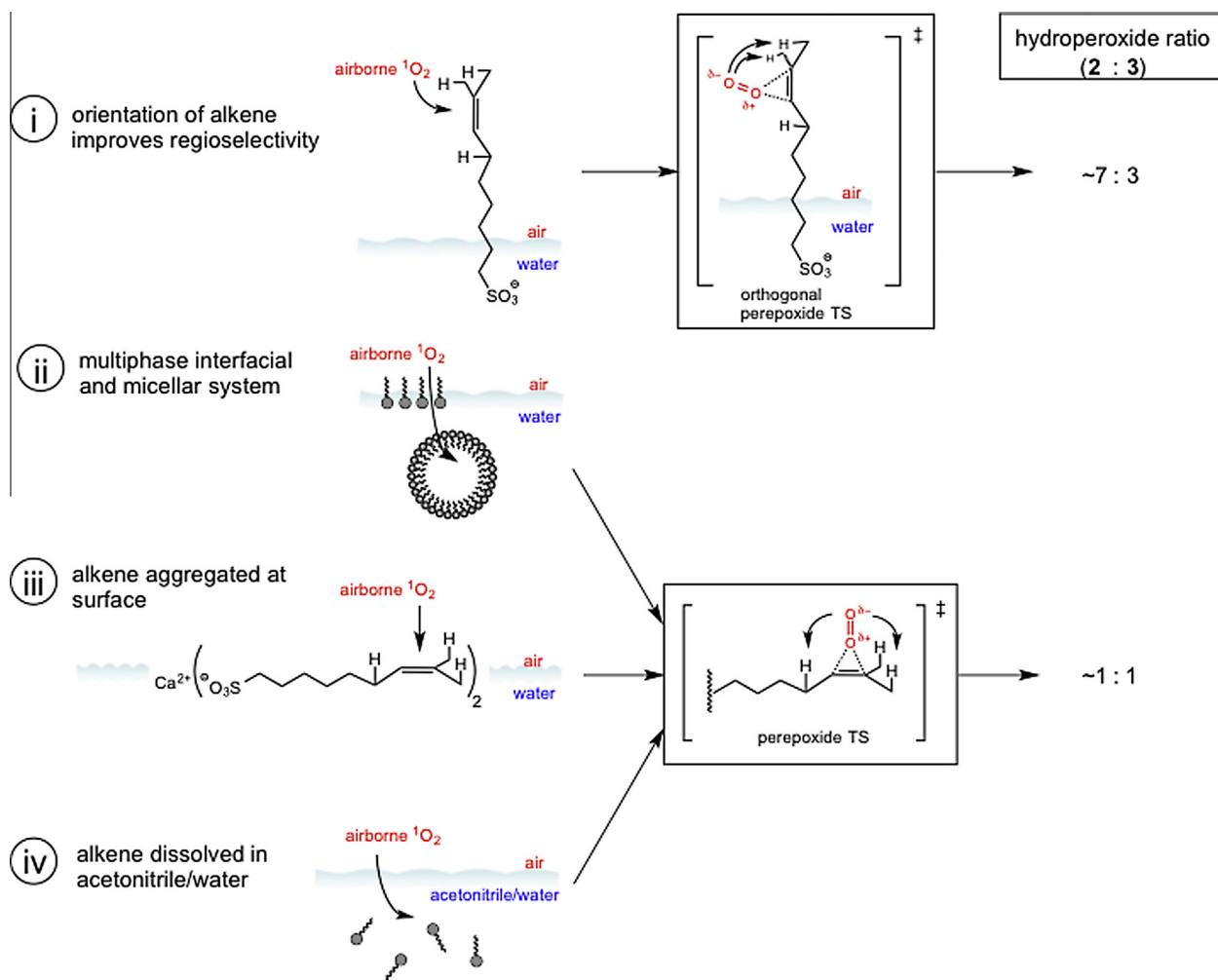
Figure 2. Mechanistic summary of airborne $^1O_2$ reaction of alkene **1** at sub-micellar concentrations (i), micellar concentrations (ii), in the presence of Ca^{2+} ions (iii), and dissolved in acetonitrile/water (iv).

micellization,[20] analogous to 2-methyl-2-pentene in homogeneous solution.[8]

Our data in Table 1 also led us to seek alternative explanations for the regioselectivity seen in entries 1 and 2. Notably, there are reports where secondary and tertiary hydroperoxides can decompose at different rates when encapsulated in zeolites.[21] Control reactions showed that **2** and **3** did not decompose under the reaction conditions prior to quantification. The hydroperoxides were stable for several days at room temperature, where after 1 h, **2** decomposed completely at $100 \pm 3\ °C$, and **3** decomposed completely at $185 \pm 5\ °C$. Because allylic hydroperoxides can rearrange thermally by O_2 shift in a radical rearrangement, that is, the Schenck mechanism,[22] we further examined the stability of **2** and **3** toward isotope exchange of $^{18}O_2$ for introduction of the ^{18}O-labels. However, oxygen sparging with ^{18}O-labeled O_2 in solution produced no hydroperoxide mass increase of 4 amu based on LCMS data. Thus, the regioselectivity is inconsistent with a mechanism that involves a hydroperoxy radical rearrangement.

Conclusion

Thus, we have developed a phase-separated reaction, where regioisomer **2** is favored at the air–water interface by the orientation of the alkene methyls toward incoming (airborne) $^1O_2$ in dilute solution of **1**. The origin of the selectivity is an unequally wetted

alkene in this synthetic process. The delivery of airborne $^1O_2$ to the alkene site aggregated at the interface or in a micelle or dissolved in acetonitrile/water showed no selectivity. Future studies will be needed for a deeper understanding of conformational properties of this $^1O_2$ ene reaction at the interface, such as dynamics of the alkene group and tilting,[23] as well as possible selectivity dependence on the alkene sulfonate chain length.

Acknowledgments

Supplementary data

Supplementary data (reagents, synthetic, instrumental and experimental details) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.05.111.

References and notes

1. (a) Griffith, E. C.; Tuck, A. F.; Vaida, V. *Acc. Chem. Res.* **2012**, *45*, 2106–2113; (b) Vaida, V.; Tuck, A. F. In *Water and Life: The Unique Properties of H₂O*; Lindon-Bell,

R. M.; Morris, S. C.; Barrow, J. D.; Finney, J. L.; Harper, Jr., C. L., Eds.; CRC Press, Taylor and Francis, 2010; pp 235–247.

2. Lemarchand, A.; Jullien, L. *J. Phys. Chem. B* **2004**, *108*, 11782–11791.
3. (a) Wang, S.; Wang, T.; Ding, Y.; Su, Q.; Xu, Y.; Xu, Z.; Jiang, G.; Chen, W. *Sci. Adv. Mater.* **2013**, *5*, 1006–1012; (b) Aebisher, D.; Bartusik, D.; Liu, Y.; Zhao, Y.; Barahman, M.; Xu, Q.; Lyons, A. M.; Greer, A. *J. Am. Chem. Soc.* **2013**, *135*, 18990–18998; (c) Sautrey, G.; Clarot, I.; Salem, A. B.; Rogalska, E. *New J. Chem.* **2012**, *36*, 78–85; (d) King, M. D.; Rennie, A. R.; Thompson, K. C.; Fisher, F. N.; Dong, C. C.; Thomas, R. K.; Pfrang, C.; Hughes, A. V. *Phys. Chem. Chem. Phys.* **2009**, *35*, 7699–7707; (e) Kotsovolou, S.; Chiou, A.; Verger, R.; Kokotos, G. *J. Org. Chem.* **2001**, *66*, 962–967; (f) Chiou, A.; Markidis, M.; Constantinou-Kokotou, V.; Verger, R.; Kokotos, G. *Org. Lett.* **2000**, *2*, 347–350.
4. (a) Ouchi, A.; Hyugano, T.; Kaneda, M.; Suzuki, T.; Liu, C. *J. Flow Chem.* **2014**, *4*, 190–194; (b) Gawande, M. B.; Bonifacio, V. D.; Luque, R.; Branco, P. S.; Varma, R. S. *Chem. Soc. Rev.* **2013**, *42*, 5522–5551; (c) Rao, C. N. R.; Kalyanikutty, K. P. *Acc. Chem. Res.* **2008**, *41*, 489–499; (d) Wang, M. L.; Lee, Z. F. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 80–87; (e) Morales, J.; Zanocco, A. L.; Günther, G.; Lemp, E. *J. Chromatogr., A* **2006**, *25*, 89–94; (f) Battal, T.; Rathman, J. F. *Surfactant Sci. Ser.* **2001**, *100*, 359–371.
5. (a) Marfil, M.; Albericio, F.; Alvarez, M. *Tetrahedron* **2004**, *60*, 8659–8668; (b) Wolf, S.; Foote, C. S.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 7770–7771; (c) Rebek, J., Jr.; Brown, D.; Zimmerman, S. *J. Am. Chem. Soc.* **1975**, *97*, 454–455; (d) Rebek, J., Jr.; Gavina, F. *J. Am. Chem. Soc.* **1975**, *97*, 3453–3456.
6. Choudhury, R.; Greer, A. *Langmuir* **2014**, *30*, 3599–3605.
7. A bubbling system was also reported: Bartusik, D.; Aebisher, D.; Lyons, A. M.; Greer, A. *Environ. Sci. Technol.* **2012**, *46*, 12098–12104.
8. Manring, L. E.; Foote, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 4710–4717.
9. (a) Orfanopoulos, M.; Stratakis, M.; Elemes, Y. *J. Am. Chem. Soc.* **1990**, *112*, 6417–6418; (b) Clennan, E. L.; Chen, X. *J. Org. Chem.* **1988**, *53*, 3124–3126.
10. (a) Snead, D.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2014**, *53*, 983–987; (b) He, Z.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2014**, *53*, 3353–3357; (c) Ronzani, F.; Saint-Cricq, P.; Arzoumanian, E.; Pigot, T.; Blanc, S.; Oelgemöller, M.; Oliveros, E.; Richard, C.; Lacombe, S. *Photochem. Photobiol.* **2014**, *90*, 358–368; (d) Tucker, J. W.; Zhang, Y.; Jamison, T. F.; Stephenson, C. R. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 4144–4147; (e) Terao, K.; Nishiyama, Y.; Tanimoto, H.; Oelgemöller, M.;

Morimoto, T. *J. Flow Chem.* **2012**, *2*, 73–76; (f) Aida, S.; Terao, K.; Nishiyama, Y.; Kakiuchi, K.; Oelgemöller, M. *Tetrahedron Lett.* **2012**, *53*, 5578–5581; (g) Yavorskyy, A.; Shvydkiv, O.; Nolan, K.; Hoffmann, N.; Oelgemöller, M. *Tetrahedron Lett.* **2011**, *52*, 278–280; (h) Pimparkar, K.; Yen, B.; Goodell, J.; Martin, V.; Lee, W.-H.; Porco, J.; Beeler, A.; Jensen, K. *J. Flow Chem.* **2011**, *1*, 53–55; (i) Vasudevan, A.; Villamil, C.; Trumbull, J.; Olson, J.; Sutherland, D.; Pan, J.; Djuric, S. *Tetrahedron Lett.* **2010**, *51*, 4007–4009; (j) Sugimoto, A.; Fukuyama, T.; Sumino, Y.; Takagi, M.; Ryu, I. *Tetrahedron* **2009**, *65*, 1593–1598.
11. Midden, W. R.; Wang, S. Y. *J. Am. Chem. Soc.* **1983**, *105*, 4129–4145.
12. (a) Doane, T. L.; Chuang, C. H.; Chomas, A.; Burda, C. *ChemPhysChem* **2013**, *14*, 321–330; (b) Nyokong, T. *Coord. Chem. Rev.* **2007**, *251*, 1707–1722.
13. (a) Jensen, R. L.; Arnbjerg, J.; Ogilby, P. R. *J. Am. Chem. Soc.* **2010**, *132*, 8098–8105; (b) Lindig, B. A.; Rodgers, M. A. *J. Photochem. Photobiol.* **1981**, *33*, 627–634.
14. (a) Hurst, J. R.; Schuster, G. B. *J. Am. Chem. Soc.* **1983**, *109*, 5756–5760; (b) Rodgers, M. A. *J. Am. Chem. Soc.* **1983**, *109*, 6201–6205; (c) Schmidt, R.; Brauer, H.-D. *J. Am. Chem. Soc.* **1983**, *109*, 6976–6981.
15. Singleton, D. A.; Hang, C.; Szymanski, M. J.; Meyer, M. P.; Leach, A. G.; Kuwata, K. T.; Chen, J. S.; Greer, A.; Foote, C. S.; Houk, K. N. *J. Am. Chem. Soc.* **2003**, *125*, 1319–1328.
16. Sheppard, A. N.; Acevedo, O. *J. Am. Chem. Soc.* **2009**, *131*, 2530–2540.
17. Leach, A. G.; Houk, K. N.; Foote, C. S. *J. Org. Chem.* **2008**, *73*, 8511–8519.
18. Lissi, E. A.; Encinas, M. V.; Lemp, E.; Rubio, M. A. *Chem. Rev.* **1993**, *93*, 699–723.
19. Lissi, E. A.; Rubio, M. A. *Pure Appl. Chem.* **1990**, *62*, 1503–1510.
20. (a) Memon, M. K.; Shuker, M. T.; Elraies, K. A. *J. Appl. Sci.* **2014**, *14*, 3339–3343; (b) Rosen, M. J.; Kunjappu, J. T. *Surfactants Interfacial Phenomena*, 4th ed.; Wiley: New York, 2012. pp 132–140.
21. (a) Stratakis, M.; Raptis, C.; Sofikiti, N.; Tsangarakis, C.; Kosmas, G.; Zaravinos, I.-P.; Kalaitzakis, D.; Stavroulakis, D.; Baskakis, C.; Stathoulopoulou, A. *Tetrahedron* **2006**, *62*, 10623–10632; (b) Kaanumalle, L. S.; Shailaja, J.; Robbins, R. J.; Ramamurthy, V. *J. Photochem. Photobiol., A* **2002**, *153*, 55–65.
22. (a) Davies, A. G. *J. Chem. Res.* **2009**, *9*, 533–544; (b) Ohtani, B.; Nishida, M.; Nishimoto, S. I.; Kagiya, T. *Photochem. Photobiol.* **1986**, *44*, 725–732.
23. Czajka, A.; Hazell, G.; Eastoe, J. *Langmuir* **2015**. http://dx.doi.org/10.1021/acs.langmuir.5b00336.