

Fabrication of Unique Chemical Patterns and Concentration Gradients with Visible Light

Brett P. Fors, Justin E. Poelma, Matthew S. Menyo, Maxwell J. Robb, Daniel M. Spokoyny, John W. Kramer, J. Herbert Waite, and Craig J. Hawker*

Materials Research Laboratory, California NanoSystems Institute, Materials Department, Department of Chemistry and Biochemistry, and Biomolecular Science and Engineering, University of California, Santa Barbara, California 93106, United States

The Dow Chemical Company, Midland, Michigan 48667, United States

S Supporting Information

ABSTRACT: A modular and general method based on a photomediated ATRA reaction for the spatially controlled functionalization of surfaces with visible light is reported. The ability to control reactivity with light intensity combined with the orthogonality of ATRA chemistry allows well-defined chemically differentiated monolayers and complex nonlinear chemical concentration gradients to be easily prepared. Use of light to mediate these reactions permits spatial regulation and the generation of unique, multifunctional chemical gradients.

The spatial arrangement of functional groups at surfaces and interfaces is of paramount importance in a variety of research areas such as antifouling, biological assays, and block copolymer self-assembly for next-generation microelectronic devices.^{1–4} The continued growth of these areas is driving the further development and refinement of patterning methods that lead to spatially defined chemical functionalities, with the most versatile and widely used procedures including microcontact printing,^{5–7} lithography (i.e., electron-beam, scanning probe, photo, etc.),^{8–12} diffusion strategies,^{13–16} or photomediated reactions.^{17–25} While these methods are successful for simple patterns from a single functional group, the generation of more complex, multifunctional surfaces remains a challenge.

Arguably, the most challenging surface structures are chemical concentration gradients, which are becoming an increasingly important class of patterned monolayers.²⁶ While microcontact printing^{5,6} and vapor deposition¹⁴ can lead to gradients, procedures are often complicated and lead to poorly defined, macro-scale features. The most successful recent example is the work of Becker who developed a “vacuum away” deposition procedure that enables the fabrication of gradients containing orthogonal functional groups.¹⁵ However, this method is limited to linear chemical gradients over relatively large distances (cm scale). Accordingly, a system that could create complex, nonlinear chemical concentration gradients from a diverse set of functional groups over a range of length scales (μm to cm) would be of considerable value.

We recently reported a method for the fabrication of three-dimensional poly(methyl methacrylate) brushes on surfaces²⁷ using a photomediated radical polymerization procedure.²⁸ Due to the short excited-state lifetime of the Ir catalyst, excellent spatial resolution and a high degree of temporal control over

brush growth were observed. We envisaged that the combination of this short excited-state lifetime with photo-mediated atom-transfer radical addition (ATRA) chemistry would enable unprecedented control for patterning molecular layers at surfaces.

The key to addressing this challenge was visible-light-mediated Ir-catalyzed ATRA chemistry developed by Stephenson and co-workers.^{29,30} We hypothesized that this chemistry would enable the photopatterning of a diverse range of molecules containing pendent alkene substituents starting from an alkyl bromide functionalized surface (Figure 1a). Notably,

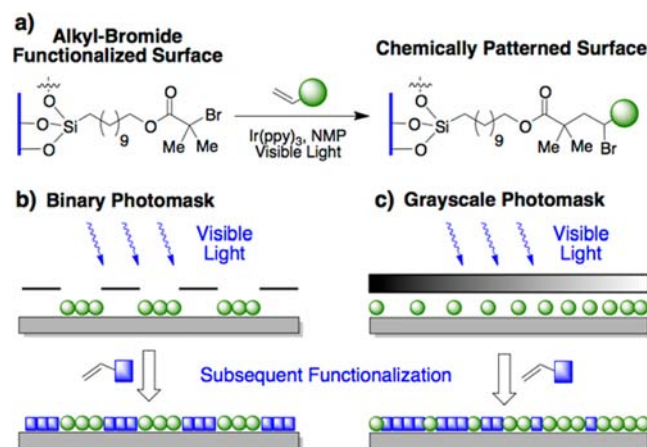


Figure 1. Multistep photomediated atom-transfer radical addition reactions for the patterning of multiple functional groups at surfaces.

using a binary photomask, surface modification would only occur in irradiated regions (Figure 1b). Moreover, irradiation through a grayscale mask would yield complex gradients where the chemical concentration on the surface would be proportional to the dosage of incident light (Figure 1c).³¹ Equally important is the facile nature of the ATRA reaction which leaves the alkyl bromide groups intact in the non-irradiated areas and, therefore, available for subsequent ATRA steps with different functional units. The combination of these features would furnish a general procedure for patterning multifunc-

Received: August 15, 2013

Published: September 11, 2013

tional chemically differentiated regions, as well as complex nonlinear chemical concentration gradients.

To evaluate this hypothesis, we began by investigating the patterning of a reactive *N*-hydroxysuccinimide (NHS) ester derived from the nonactivated, terminal alkene (**1**). A silicon oxide surface, uniformly functionalized with an alkyl bromide, was layered with a solution of **1** and Ir(ppy)₃ in *N*-methylpyrrolidinone (NMP) and irradiated with a 50 W fluorescent lamp through a photomask comprised of 20 × 200 μm rectangles for 30 min (Figure 1a). The NHS-ester-functionalized surface was then treated with an amino-substituted coumarin dye (**2**) to allow visualization of the pattern. The fluorescence micrograph in Figure 2b clearly

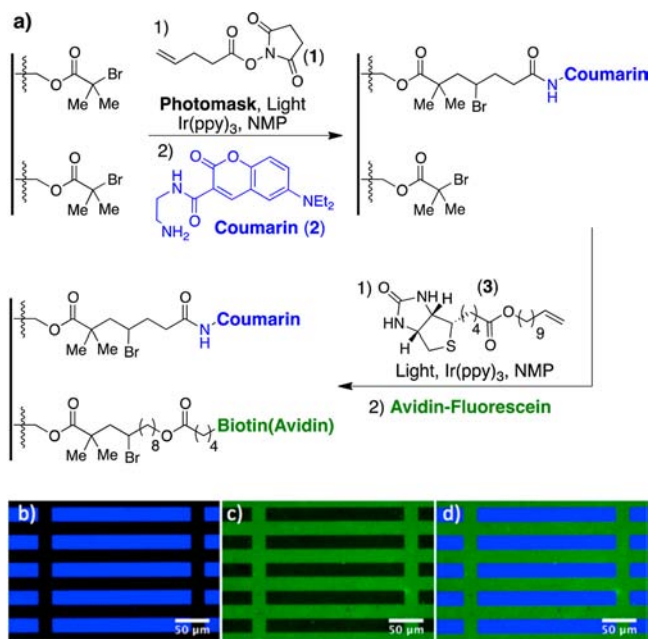


Figure 2. Fabrication of chemically differentiated areas on a surface with light using a binary photomask.

shows functionalization occurred only where the light reached the substrate and reveals that good spatial resolution can be obtained using this photomediated ATRA reaction for patterning. Notably, features down to 1 μm have been successfully patterned using this method (see Supporting Information).³²

A powerful aspect of the ATRA reaction is the orthogonal, nondestructive nature of the Ir-catalyzed process. As a result, the unexposed grid region of the surface surrounding the coumarin-functionalized rectangles in Figure 2b still contains reactive alkyl bromide groups which may be available for secondary derivatization. The same substrate was then exposed to a solution of the biotin functionalized alkene (**3**) and Ir(ppy)₃ in NMP and blanket irradiated with visible light (i.e., no photomask). Following treatment with fluorescein labeled avidin, fluorescence microscopy (Figure 2c) demonstrated that controlled reaction of **3** only occurred in the previously unexposed region of the substrate. Further, the overlay of the coumarin and fluorescein channels displays no overlapping of the two chemical domains even though no photomask was used in the second functionalization step (Figure 2d). This result establishes the quantitative nature of the initial patterning step and the ability to generate well-defined chemically differentiated regions. Moreover, the use of biotin–avidin illustrates

that this method is applicable to biologically relevant systems and can be used to spatially arrange proteins on a surface.

To further highlight the functional group tolerance of the ATRA chemistry and the generality of this methodology, catechol functional groups were patterned onto a surface and then used to template the self-assembly of iron oxide nanoparticles (Figure 3). In an analogous fashion to the

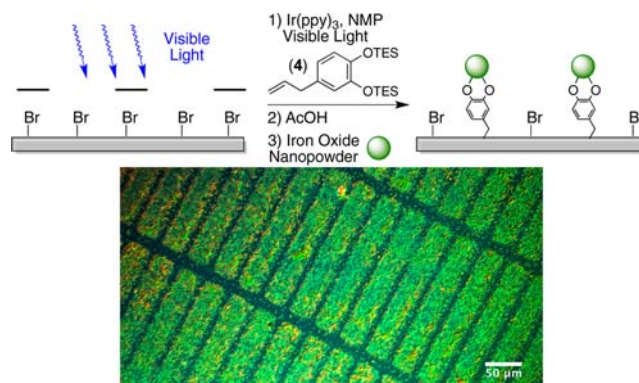


Figure 3. Templated assembly of iron oxide nanoparticles facilitated by the patterning of catechol functional groups on a surface.

procedure above, a silyl-protected catechol (**4**)³³ was patterned using the photomask containing 20 × 200 μm rectangles. The catechol was then deprotected and treated with a suspension of iron oxide nanoparticles (<50 nm) in ethanol. After washing, a polarized optical micrograph of the surface revealed the nanoparticles had efficiently bound to the catechol functionalized areas of the substrate. This result emphasizes the facile nature of this approach with catechol units typically being prone to side reactions under a variety of conditions. In addition, the ability to use a wide variety of nonactivated alkenes or alkynes demonstrates the modularity and generality of this approach for tailoring surface properties.

Having established the capability to pattern micrometer-sized features and the quantitative nature of the functionalization process, the next major challenge was to investigate this method for the formation of well-controlled concentration gradients. In solution, the rate of these ATRA reactions is directly proportional to the intensity of irradiated light. Therefore, we reasoned that modulating the amount of light that reached the surface would allow the extent of reaction and hence, functional group density, to be precisely controlled. To test this hypothesis, a grayscale photomask containing 100 × 100 μm squares that varied linearly in transmittance (from 0.6 to 0.03) across the feature was employed.³¹ Using conditions described above with irradiation through these grayscale masks for 10 min, the NHS ester **1** was reacted with the surface followed by derivatization with an amino-substituted fluorescein dye for evaluation of the feature. The fluorescence micrograph in Figure 4a and the three-dimensional representation of these data in Figure 4b, where the *z*-axis is photoluminescence (PL) intensity, distinctly show the chemical concentration gradient of fluorescein on the surface. This result confirms that regulating the dosage of irradiated light can modulate the chemical density on the surface.

To further demonstrate that the rate of reaction on the surface can be precisely adjusted, we prepared four separate fluorescein patterns using photomasks with different optical gradients. Each grayscale mask varied linearly in transmittance

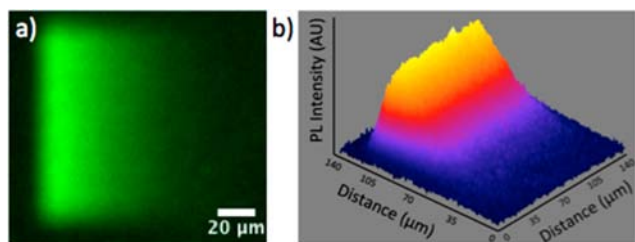


Figure 4. Fluorescence microscopy images of a chemical concentration gradient of fluorescein that was fabricated using a grayscale photomask.

and had the same starting value (0.60) but varying end values (0.55, 0.34, 0.18, and 0.03). After patterning, the cross sections of each of the chemical features display a clear correlation between the transmittance gradient of the mask and the density of the dye on the surface (Figure 5a-d, respectively). These

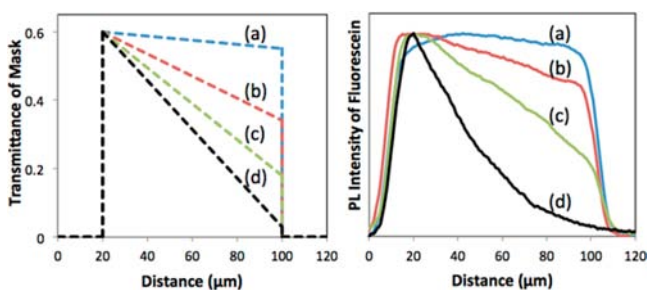


Figure 5. Cross section of four separate chemical concentration gradients of fluorescein made using grayscale masks with differing slopes of transmittance (a) - 0.60 to 0.55; (b) - 0.60 to 0.34; (c) - 0.60 to 0.18 and (d) - 0.60 to 0.03.

results demonstrate that the areal density of chemical functionalization on the surface can be readily controlled on the micrometer scale by simple modulation of light intensity using standard photomasks.

In an analogous manner to the previous experiments that used a binary photomask, the alkyl bromides that were not consumed in the initial reaction after patterning with a grayscale mask are still available for further functionalization. To exploit this feature we used our standard procedure to pattern a concentration gradient of fluorescein using a photomask that varied linearly in optical density. Subsequent blanket irradiation allows the remaining alkyl bromides, which now have a density profile inverse to the original gradient, to be reacted with **1** and then substituted with the coumarin-based dye (**2**) for visualization. The resulting surface contains two inverse chemical concentration gradients that could be readily observed by fluorescence microscopy (Figure 6). A cross-section of this pattern reveals that the concentration of coumarin decreases as the concentration of fluorescein increases. This dual concentration profile for a multifunctional surface illustrates the potential of this technique and the unique structures that can be prepared.

One of the advantages of this methodology is the high level of control that can be achieved through light modulation when compared to other external means of chemical regulation.³⁴ This allows for the facile formation of complex nonlinear gradients. To demonstrate this concept, the active ester **1** was patterned using a grayscale photomask containing an array of positive lenses (followed by functionalization with fluorescein). Each lens is 50 μm in diameter and varies radially from its

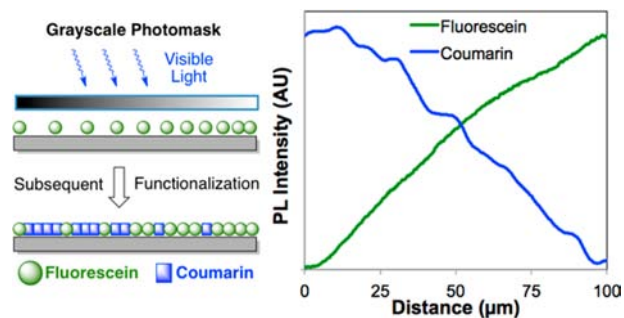


Figure 6. Dual chemical concentration gradients of coumarin and fluorescein.

center in optical density. Fluorescence microscopy of the final substrate clearly illustrates that the lens pattern was transferred to the surface with the fluorescein concentration decreasing radially from the center of each feature (Figure 7a). Moreover,

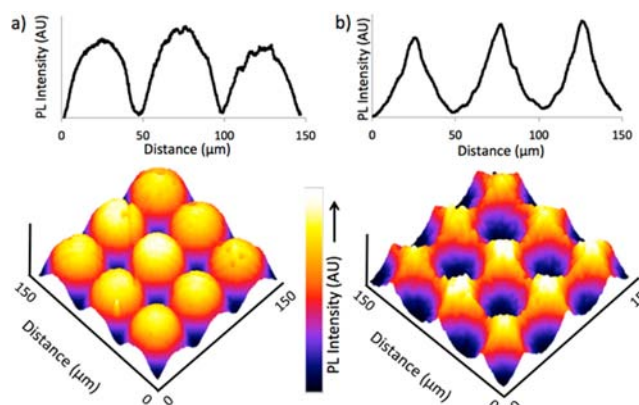


Figure 7. Synthesis of complex nonlinear chemical concentration gradients of fluorescein with a grayscale mask containing an array of (a) positive and (b) negative lenses.

using the inverse mask with negative lenses yielded a similar structure where, in contrast to the previous experiment, the fluorescein density *increases* radially from the center of each feature (Figure 7b). These experiments confirm that this method can be used to fabricate complex chemical concentration gradients that are not accessible using alternative patterning methods, such as deposition techniques.

In summary, a general and modular approach for surface patterning using photomediated ATRA chemistry has been developed. The power of this ATRA strategy lies in its compatibility with a wide variety of functional groups coupled with the ability to tune the location and density of functionalization by modulating the dosage of visible light. Complex, nonlinear chemical concentration gradients and patterned multifunctional surfaces that cannot be prepared using traditional approaches are now possible. We expect that the simplicity of this method and its ability to pattern a diverse set of functional molecules will make it a practical tool for a wide range of applications.

■ ASSOCIATED CONTENT

📄 Supporting Information

Experimental procedures, compound characterization data, and further patterning examples. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

hawker@mrl.ucsb.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the MRSEC program of the National Science Foundation (DMR 1121053) and the Dow Chemical Co. through the Dow Materials Institute at UCSB for financial support. B.P.F. thanks the California NanoSystems Institute for the Elings Prize Fellowship in Experimental Science. J.E.P. thanks the NSF Graduate Research Fellowship for funding. M.J.R. thanks UC Regents, CSP Technologies, and the DOE Office of Science (DOE-SCGF) for graduate fellowships.

■ REFERENCES

- (1) Andruzzi, L.; Nickel, B.; Schwake, G.; Rädler, J. O.; Sohn, K. E.; Mates, T. E.; Kramer, E. J. *Surf. Sci.* **2007**, *601*, 4984–4992.
- (2) Weinrich, D.; Jonkheijm, P.; Niemeyer, C. M.; Waldmann, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 7744–7751.
- (3) Kim, S. O.; Solak, H. H.; Stokovich, M. P.; Ferrier, N. J.; de Pablo, J. J.; Nealey, P. F. *Nature* **2003**, *424*, 411–414.
- (4) (a) Hannon, A. F.; Gotrik, K. W.; Ross, C. A.; Alexander-Katz, A. *ACS Macro Lett.* **2013**, *2*, 251–255. (b) Azzaroni, O. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 3225–3258.
- (5) Choi, S.-H.; Zhang Newby, B.-M. *Langmuir* **2003**, *19*, 7427–7435.
- (6) Bhangale, S. M.; Tjong, V.; Wu, L.; Yakovlev, N.; Moran, P. M. *Adv. Mater.* **2005**, *17*, 809–813.
- (7) Spruell, J. M.; Wolffs, M.; Leibfarth, F. A.; Stahl, B. C.; Heo, J.; Connal, L. A.; Hu, J.; Hawker, C. J. *J. Am. Chem. Soc.* **2011**, *133*, 16698–16706.
- (8) Chen, T.; Amin, I.; Jordan, R. *Chem. Soc. Rev.* **2012**, *41*, 3280–3296.
- (9) Ahn, S. J.; Kaholek, M.; Lee, W. K.; LaMattina, B.; LaBean, T. H.; Zauscher, S. *Adv. Mater.* **2004**, *16*, 2141–2145.
- (10) Ballav, N.; Schilp, S.; Zharnikov, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 1421–1424.
- (11) Khan, M. N.; Tjong, V.; Chilkoti, A.; Zharnikov, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 10303–10306.
- (12) Zhou, X.; Wang, X.; Shen, Y.; Xie, Z.; Zheng, Z. *Angew. Chem., Int. Ed.* **2011**, *50*, 6506–6510.
- (13) Chaudhury, M. K.; Whitesides, G. M. *Science* **1992**, *256*, 1539–1541.
- (14) Albert, J. N. L.; Baney, M. J.; Stafford, C. M.; Kelly, J. Y.; Epps, T. H., III *ACS Nano* **2009**, *3*, 3977–3986.
- (15) Ma, Y.; Zheng, J.; Amond, E. F.; Stafford, C. M.; Becker, M. L. *Biomacromolecules* **2013**, *14*, 665–671.
- (16) Beurer, E.; Venkataraman, N. V.; Rossi, A.; Bachmann, F.; Engeli, R.; Spencer, N. D. *Langmuir* **2010**, *26*, 8392–8399.
- (17) Tasdelen, M. A.; Yagci, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 5930–5938.
- (18) Zubir, El, O.; Barlow, I.; Ul-Haq, E.; Tajuddin, H. A.; Williams, N. H.; Leggett, G. J. *Langmuir* **2013**, *29*, 1083–1092.
- (19) Pauloeherl, T.; Delaittre, G.; Bruns, M.; Meißler, M.; Börner, H. G.; Bastmeyer, M.; Barner-Kowollik, C. *Angew. Chem., Int. Ed.* **2012**, *51*, 9181–9184.
- (20) Orski, S. V.; Poloukhina, A. A.; Arumugam, S.; Mao, L.; Popik, V. V.; Locklin, J. *J. Am. Chem. Soc.* **2010**, *132*, 11024–11026.
- (21) Weinrich, D.; Köhn, M.; Jonkheijm, P.; Westerlind, U.; Dehmelt, L.; Engelkamp, H.; Christianen, P. C. M.; Kuhlmann, J.; Maan, J. C.; Nüsse, D.; Schröder, H.; Wacker, R.; Voges, E.; Breinbauer, R.; Kunz, H.; Niemeyer, C. M.; Waldmann, H. *ChemBioChem* **2009**, *11*, 235–247.
- (22) Gallant, N. D.; Lavery, K. A.; Amis, E. J.; Becker, M. L. *Adv. Mater.* **2007**, *19*, 965–969.
- (23) Khire, V. S.; Benoit, D. S. W.; Anseth, K. S.; Bowman, C. N. J. *Polym. Sci. A: Polym. Chem.* **2006**, *44*, 7027–7039.
- (24) Pauloeherl, T.; Delaittre, G.; Winkler, V.; Welle, A.; Bruns, M.; Börner, H. G.; Greiner, A. M.; Bastmeyer, M.; Barner-Kowollik, C. *Angew. Chem., Int. Ed.* **2011**, *51*, 1071–1074.
- (25) Arumugam, S.; Popik, V. V. *J. Am. Chem. Soc.* **2011**, *133*, 15730–15736.
- (26) Genzer, J. *Annu. Rev. Mater. Res.* **2012**, *42*, 435–468.
- (27) Poelma, J. E.; Fors, B. P.; Meyers, G. F.; Kramer, J. W.; Hawker, C. J. *Angew. Chem., Int. Ed.* **2013**, *52*, 6844–6848.
- (28) Fors, B. P.; Hawker, C. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 8850–8853.
- (29) Nguyen, J. D.; Tucker, J. W.; Konieczynska, M. D.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2011**, *133*, 4160–4163.
- (30) Wallentin, C.-J.; Nguyen, J. D.; Finkbeiner, P.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2012**, *134*, 8875–8884.
- (31) Kley, E.-B.; Thoma, F.; Zeitner, U. D.; Wittig, L.; Aagedal, H. *SPIE* **1998**, *3276*, 254–262.
- (32) See Supporting Information for details.
- (33) Heo, J.; Kang, T.; Jang, S. G.; Hwang, D. S.; Spruell, J. M.; Killops, K. L.; Waite, J. H.; Hawker, C. J. *J. Am. Chem. Soc.* **2012**, *134*, 20139–20145.
- (34) Leibfarth, F. A.; Mattson, K. M.; Fors, B. P.; Collins, H. A.; Hawker, C. J. *Angew. Chem., Int. Ed.* **2013**, *52*, 199–210.