Organic LETTERS

Letter

Cite This: Org. Lett. XXXX, XXX, XXX-XXX

pubs.acs.org/OrgLett

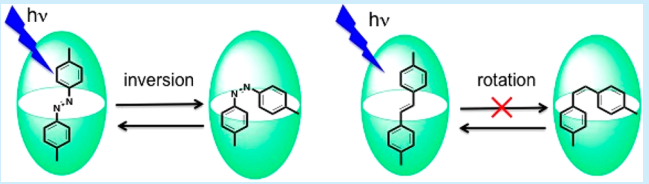
Volume Conserving Geometric Isomerization of Encapsulated Azobenzenes in Ground and Excited States and as Radical Ion

A. Mohan Raj and V. Ramamurthy*

Department of Chemistry, University of Miami, Coral Gables, Florida 33124, United States

Supporting Information

ABSTRACT: To probe the role of the supramolecular steric effects and free volume on photoreactions, geometric isomerization of neutral azobenzenes (ABs) and their radical ions, generated by electron transfer with gold nanoparticles, included within an octa acid capsule, was investigated. A comparison of the isomerization of ABs that proceed by volume conserving pyramidalization and stilbene analogues that proceed by volume demanding one bond flip has indicated the differing influence of 4-alkyl groups on these two processes.



To establish the disparate, selective behavior of "contained and constrained" molecules from the free ones, we have explored the excited state behavior of organic molecules within a bimolecular organic capsule of the cavitand octa acid (OA, Figure 1).[1] Our exploration of geometric isomerization of stilbenes and

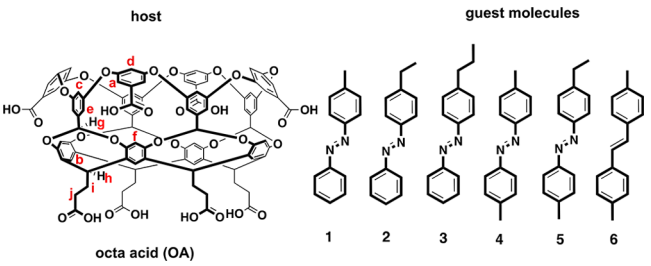


Figure 1. Structures of host and guest molecules.

GFP chromophores revealed that their excited state behavior within a capsule could only be predicted by considering the overall structure of a host–guest complex and not that of the free guest.[2−4] As geometric isomerization in these olefins proceeds, via the volume demanding 180° bond flip, we examined the effect of constraint on the alternate volume conserving geometric isomerization process, namely, pyramidalization. Geometric isomerization of azobenzene (AB) in the excited and ground states, occurring through the pyramidalization mechanism, made it an ideal choice to examine the influence of constraints and containment.[5,6] Radical anion of *cis*-AB generated by electron transfer (eT) was also reported to isomerize swiftly via pyramidalization and progress by a chain mechanism.[7] Our earlier studies establishing the feasibility of eT between a donor and an acceptor separated by the OA capsular wall gave us the confidence to generate the source *cis*-AB radical ion within a capsule.[8,9] In this study, gold nanoparticles (AuNPs) known to act as an electron source and sink in the dark were employed to generate AB radical ion.[10] We hoped our studies using OA capsule would determine the yet to be fully unraveled mechanism of AuNP-catalyzed geometric isomerization of *cis*-AB. The current study afforded the examination of the geometric isomerization of AB in the ground and excited states as well as that of AB radical ion in the dark and the behavior of AB relative to the volume demand, with one bond flip isomerization of stilbene analogues. The results of the thermal isomerization of AB and its radical ion and the photochemical isomerization of AB are presented below.

Trans-azobenzenes **1**−**5** (Figure 1) were synthesized, purified, and characterized by methods reported in the literature.[11,12] Complexation of **1**−**5** with OA in aqueous solution was achieved as outlined in the Supporting Information. Characteristic changes in the ^{1}H NMR signals of the host OA and the upfield shifts of the signals due to *para*-alkyl groups (CH_2 and CH_3) of the guest (note signals in the region of δ 5.5−8 and below 0 ppm, respectively, in Figure 2) in the $Na_2B_4O_7$−D_2O solution

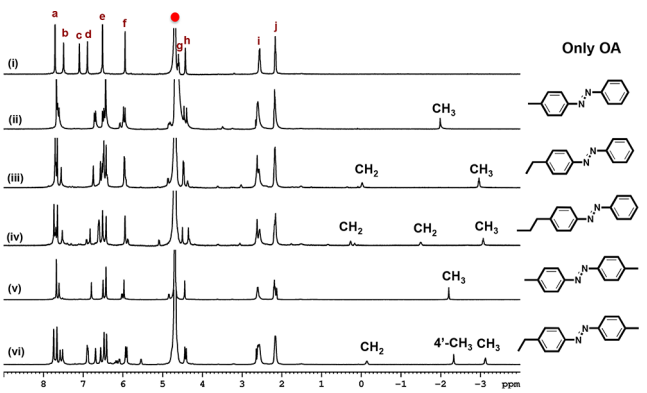


Figure 2. ^{1}H NMR (500 MHz) spectra of (i) OA only, (ii) **1**@OA_2, (iii) **2**@OA_2, (iv) **3**@OA_2, (v) **4**@OA_2, and (vi) **5**@OA_2 ([OA] = 1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O [**1**−**5**] = 0.5 mM; the red dot represents the residual D_2O.

Received: September 21, 2017

DOI: 10.1021/acs.orglett.7b02963
Org. Lett. XXXX, XXX, XXX−XXX

containing **1**−**5** and OA confirmed the inclusion of the former within OA.[13,14] The continuous change in the ^{1}H NMR spectra with addition of the guest to the OA solution that ended with 0.5 equiv of the guest suggested ABs formed stable 1:2 complexes with OA (guest@OA_2) (Figures S1−S5). Absence of any signals due to the uncomplexed guest and appearance of guest peaks at the same position independent of the host/guest ratio suggested that the complex is stable in the NMR time scale. DOSY experiments measuring the diffusion constants (Table S1) of the complexes confirmed the 1:2 guest/host ratio.[13] The lack of exchange between complexed and free guests was evident from the absence of signals due to the latter during titration. Despite being insoluble in water, **1**−**5** formed a clear transparent solution as complexes of OA.

Absorption spectra of all *trans*-AB@OA_2 complexes had two maxima in the UV (350 ± 10 nm, $\pi\pi^*$) and another in the visible region (440 ± 10 nm, $n\pi^*$) (Figure S6)[15] along with absorption due to OA being below 300 nm. OA complexes of **1**−**5** in $Na_2B_4O_7$ buffer solutions were irradiated with UV light (350 ± 20 nm, Luzchem reactor) for 30 min, and the progress of the isomerization was monitored by their UV−vis absorption and ^{1}H NMR spectra. To reverse the isomerization following the generation of the *cis* isomer, the samples were irradiated with visible light (420 ± 20 nm, Luzchem reactor). The ^{1}H NMR spectra of **3** irradiated with UV and then visible light are presented in Figure 3 and those of the others in Figures S7−S10.

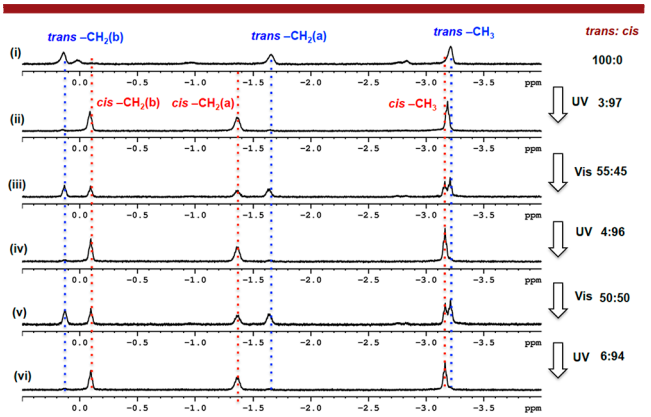


Figure 3. Photoisomerization of **3**@OA_2 monitored by ^{1}H NMR ([OA] = 1 mM in D_2O borate buffer [**3**] = 0.5 mM); NMR recorded after UV (350 ± 20 nm) and visible (420 ± 20 nm) irradiation; each irradiation is for 30 min.

Following UV irradiation of the complexes, the observed stronger and weaker absorption in the visible and UV regions were consistent with the new signals in the ^{1}H NMR spectra due to the *cis* isomers. These signals in the upfield (<δ 0) region in the ^{1}H NMR spectra confirmed the *cis* isomer's presence within the OA capsule. The photostationary state composition of *cis* and *trans* isomers under UV irradiation conditions consisted of major amounts of the *cis* (68−97%) and minor amounts of the *trans* isomers (Table 1). A photostationary state isomer ratio comparison under identical irradiation conditions in the presence and absence of OA (aqueous solution and toluene, respectively) (Table 1) suggested the effect of the substituent on the 4-position of AB to be much smaller than in the case of stilbenes (Table 1). Irradiation of the above solutions of host−guest complexes containing a photostationary state mixture of *trans* and *cis* isomers with visible light resulted in the reversal of the *cis* to the *trans* isomers (Figure 3 and Figures S7−S10).

Table 1. Photostationary State Composition of Azobenzenes 1−5 and Stilbene 6 in Solution with and without OA

compound	photostationary state in toluene (*cis*/*trans*)[a,b]	photostationary state inside OA (*cis*/*trans*)[a,b]
1	86:14	83:17
2	90:10	77:23
3	88:12	97:3
4	95:5	68:32
5	91:9	70:30
6[c]	76:18	20:80

[a]See Figure 4 for irradiation details. [b]Estimated by ^{1}H NMR. [c]From ref 2.

The difference in the influence of the capsule on the isomerization process is revealed upon comparison of the photobehavior of **4** and **6** within OA both containing 4,4′-dimethyl phenyl substituents. Unlike the *cis* isomer enrichment in isotropic solution in both cases, the photostationary mixture with **6**@OA_2 was enriched in *trans*[2] and in the *cis* isomer with **4**@OA_2. We believe nearly the same ^{1}H NMR chemical shift of the methyl groups of **6**@OA_2 and **4**@OA_2 (Figure 4), suggesting

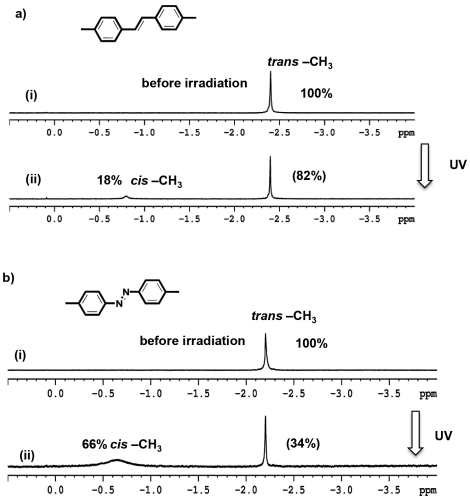


Figure 4. Partial ^{1}HNMR (500 MHz) spectra (a) (i) **6**@OA_2 before irradiation; (ii) **6**@OA_2 after 30 min UV (>280 nm); (b) (i) **4**@OA_2 before irradiation; (ii) **4**@OA_2 after 30 min UV (350 ± 20 nm); [OA] = 1 mM [**4** and **6**] = 0.5 mM.

their placement in a similar environment within OA to be from them interacting with the four aryl rings of the narrow top and bottom ends of the OA capsule. Weak CH−π interaction between the dimethyl group and the capsular wall and lack of free space around the aryl ring likely restricted the isomerization of *trans*-4,4′-dimethylstilbene to the *cis* within OA via one-bond flip, a process requiring a large sweeping motion (Figure 5).[2] Despite the two molecules' similar positioning within OA, photoisomerization of *trans*-**4** to *cis*-**4** proceeded within OA, resulting in 66% of the latter isomer in the photostationary state mixture. We trace the above variance to the mechanistic difference of the isomerization in the excited state of the two chromophores. While C═C can isomerize only by 180° rotation,[16,17] the N═N can do so by either a 180° rotation or by the volume conserving pyramidalization process.[5,6,18] As illustrated in Figure 5, the two distinct pathways require different amounts of free space around the chromophore: *trans* to *cis* conversion of **6** requires the (Ar)−C═C−(Ar) bond to sweep a larger cone through rotational

DOI: 10.1021/acs.orglett.7b02963
Org. Lett. XXXX, XXX, XXX−XXX

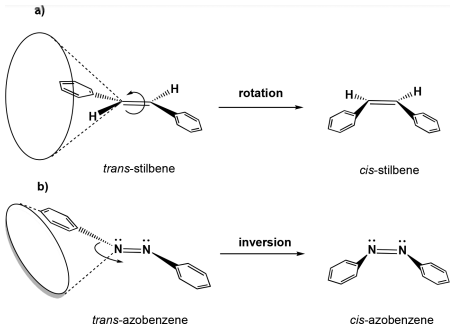


Figure 5. Mechanistic pathway for *trans*-azobenzene and *trans*-stilbene isomerization.

motion, whereas the same process in **4** is achieved via pyramidalization of the N═N chromophore that sweeps a smaller cone (Figure 5). Thus, the comparison of the above two closely related molecules in OA advocates the importance of free space within a confined reaction container and the value of such a medium in unraveling the mechanism of photoreactions.

Due to the relative thermodynamic stability of the *trans* isomer with respect to the *cis* counterpart and low activation barrier for isomerization by pyramidalization, the *cis*-ABs are well-known to isomerize from *cis* to *trans* isomers at ambient temperature in the dark.[15] The relative thermodynamic stability of the two isomers of the free AB molecules while dictated by their inherent nature would, within the OA capsule, depend on their fit within the confined space and the nature of weak interactions between the guest and the host. This is established to be the case in stilbenes. The size of the alkyl group (methyl, ethyl, and propyl) of stilbenes is found to influence the relative stability of the *cis* and *trans* isomers within OA.[19] Whereas a stronger complex was formed by *trans*-4,4′-dimethylstilbene with OA rather than the *cis* counterpart, it was the *cis*-4-ethyl/propylstilbenes rather than their *trans* isomers to do so. Both isomers of 4-methylstilbene showed equal preference. Expecting such a trend to extend to AB, which could have a significant impact on the thermal isomerization of *cis*-AB to *trans*-AB, we probed the role of these 4-alkyl groups within OA.

UV−vis absorption spectra of *cis*-**1**-**5**@OA_2 were recorded at various time intervals by keeping the solution in the dark at room temperature (Figure 6 and Figure S13). These figures reveal the time taken for the *cis*-**1**-**5**@OA_2 to isomerize to the corresponding *trans* isomers varied with the substituent on the

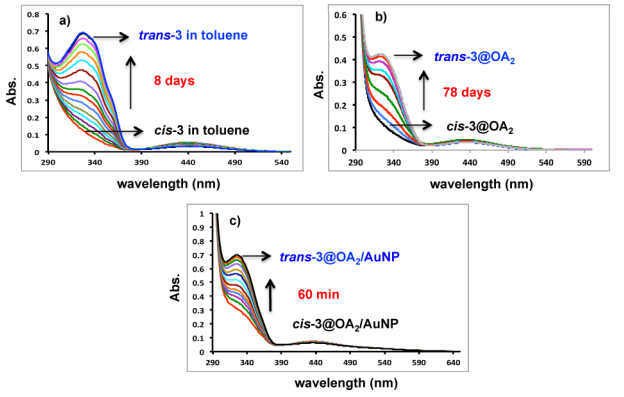


Figure 6. Absorption spectra of thermal isomerization of (a) *cis*-**3** in toluene; (b) *cis*-**3**@OA_2; and (c) *cis*-**3**@OA_2 + 200 μL of metastable AuNP ([OA] = 1×10^{-4} M, [**3**] = 0.5×10^{-4} M).

aryl ring of the AB. Whereas **1**, **4**, and **5** isomerized to the *trans* isomers within a week, **2** and **3** took a significantly longer time. The 4-propyl derivative **3** took 78 days (!) to quantitatively return to the *trans* isomer. All five *cis*-ABs in toluene and in the absence of OA quantitatively isomerized from the *cis* to the *trans* isomer in less than 8 days (Figure 6 and Figure S14), indicating the little effect that the nature of the alkyl group has on the *cis*−*trans* pyramidalization barrier in the ground state of free AB. Guided by the conclusion above that 4-ethyl and 4-propyl groups have no effect on the excited state interconversion of *cis* and *trans* isomers, we attribute the reduced *cis* to *trans* thermal isomerization rate within OA in these two examples to OA capsule's ability to modify the ground state thermodynamic stability of the included isomers. Based on the complexation behavior of stilbenes described above, we believe that among the five ABs **1**−**5**, the *cis* isomers of **2** and **3** would be relatively more stable within OA than the corresponding *trans* isomers. We surmise that the relative stability of *cis*-AB@OA_2 would translate into larger barrier and slower isomerization from *cis* to *trans* in these two cases. Most likely, *cis* isomers of **2** and **3** fit better than the *trans* within OA capsule. Such an unusual steric effect is specific to the capsule and to the alkyl substituent. Such highly selective behavior can only be observed in the case of reactions in an enzyme.

We then examined the isomerization of the −N═N− radical ion within the confined spaces of an OA capsule using AuNPs as an electron source/sink.[10] Although the catalysis of the isomerization of *cis*-AB by AuNPs has been reported, the factors governing the process has been variously attributed to (a) weakening of the −N═N− bond upon adsorption on Au surface, (b) eT from *cis*-AB to Au surface, and (c) eT from Au surface to *cis*-AB.[20−24] The confinement of *cis*-AB within OA ruling out its direct contact with the surface of AuNPs leaves the latter two options. Metastable and citrate-capped AuNPs were prepared by published procedures and characterized by their dynamic light scattering and absorption spectra (Figures S15−S18).[25−28] They had the characteristic plasmon band and possessed a diameter of 6.8 ± 2.2 nm (metastable) and 25.7 ± 2.5 nm (citrate-capped).[29,30]

To *cis*-**1**−**5**@OA_2 (2 mL, 5×10^{-5} M) was added 200 mL of AuNPs, and the absorption spectra of the solutions were recorded over time (Figures S19−S22). In most cases, the *cis* isomer was converted to *trans* within 15 min, except for *cis*-**3**@OA_2 requiring an hour. We believe that the faster isomerization from *cis* to *trans* occurred from the radical ions of AB generated via an eT process. These results illustrate AuNPs catalyzing the geometric isomerization of encapsulated *cis*-AB from a distance and without direct contact with the −N═N− bond. To the best of our knowledge, this is the first instance of an eT-induced chemical transformation of a guest molecule fully enclosed within a confined capsule. Of the five AB radical ions, the longer time taken by 4-propyl-substituted AB (60 vs 15 min) to isomerize to *trans* (Figures 6, S19, and S20), indicating greater hindrance during pyramidalization within the capsule, is consistent with the behavior of the corresponding neutral AB during the thermal isomerization in the ground state.

The final point deals with the question of whether the *cis*-AB serves as an electron donor or an acceptor with respect to AuNPs. As noted below, we have not been able to resolve this question. An early report on AuNP-catalyzed *cis* to *trans* isomerization of AB suggested generation of *cis*-AB radical cation by eT from AB to AuNP.[20] However, an electrochemically and photochemically generated AB radical anion has been demonstrated to isomerize

DOI: 10.1021/acs.orglett.7b02963
Org. Lett. XXXX, XXX, XXX−XXX

from *cis* to *trans* very quickly.[7] However, DFT calculations have suggested a lower barrier for *cis* to *trans* conversion for both AB radical anion and radical cation.[21] To probe whether the AB radical cation generated independently would lead to isomerization of *cis* to *trans*, *N*-methylacridinium iodide was selectively excited (Corning 7−60 band-pass filter, 320−400 nm) in the presence of *cis*-**3**@OA_2. Indeed, isomerization from *cis* to *trans* occurred, suggesting that the AB radical cation also preferentially isomerizes from *cis* to *trans* (Figure S23).[31,32] Thus, based on our's and literature results, one can not unequivocally state whether AB acts as the electron donor or acceptor with respect to AuNP during thermal catalytic isomerization. Further work is needed to narrow down the mechanism and identify the nature of the radical ion. We contemplate a mechanism involving eT as illustrated in Figure 7.

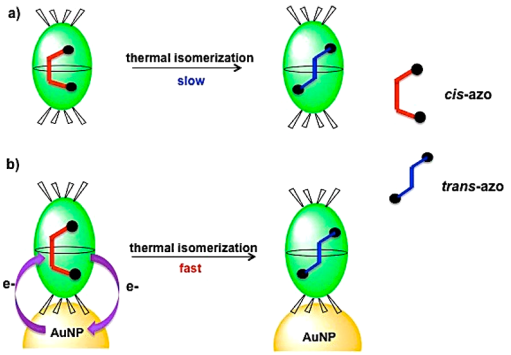


Figure 7. Cartoon representation of thermal isomerization of *cis*-ABs (a) with OA and (b) with OA in the presence of AuNPs.

The studies presented here on AB reinforce the utility of confined space in controlling reactions including the excited and ground state chemistry of neutral molecules as well as reactive intermediates. Results presented above on thermal isomerization of *cis*-azobenzenes@OA_2 to *trans* (a) highlight the importance of consideration of the structure of the host−guest complex as a whole rather than the free guest's alone in predicting the course of a reaction in confined spaces, (b) stress how minor variations in structure with no influence in isotropic solution affect the chemistry in a confined space, and (c) emphasize that the mechanism and the product formed within a supramolecular assembly are governed by the environment instead of by the intrinsic reactivity of the free molecule. The revealed possibility of eT-mediated reactions within a capsule opens new avenues which we plan to explore further.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b02963.

Experimental procedure, ^{1}H NMR spectra of the host−guest complexes, absorption and ^{1}H NMR spectra of the UV and visible light irradiated samples, AuNP-catalyzed samples and samples kept in the dark, characterization of AuNPs (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: murthy1@miami.edu.

ORCID

V. Ramamurthy: 0000-0002-3168-2185

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

V.R. thanks the National Science Foundation (CHE-1411458) for financial support.

■ REFERENCES

(1) Ramamurthy, V. *Acc. Chem. Res.* **2015**, *48*, 2904−2917.
(2) Parthasarathy, A.; Kaanumalle, L. S.; Ramamurthy, V. *Org. Lett.* **2007**, *9*, 5059.
(3) Baldridge, A.; Samanta, S. R.; Jayaraj, N.; Ramamurthy, V.; Tolbert, L. M. *J. Am. Chem. Soc.* **2010**, *132*, 1498.
(4) Baldridge, A.; Samanta, S. R.; Jayaraj, N.; Ramamurthy, V.; Tolbert, L. M. *J. Am. Chem. Soc.* **2011**, *133*, 712.
(5) Rau, H.; Lüddecke, E. *J. Am. Chem. Soc.* **1982**, *104*, 1616.
(6) Rau, H. *J. Photochem.* **1984**, *26*, 221.
(7) Goulet-Hanssens, A.; Utecht, M.; Mutruc, D.; Titov, E.; Schwarz, J.; Grubert, L.; Bléger, D.; Saalfrank, P.; Hecht, S. *J. Am. Chem. Soc.* **2017**, *139*, 335.
(8) Porel, M.; Jockusch, S.; Parthasarathy, A.; Rao, V. J.; Turro, N. J.; Ramamurthy, V. *Chem. Commun.* **2012**, *48*, 2710.
(9) Porel, M.; Chuang, C.-H.; Burda, C.; Ramamurthy, V. *J. Am. Chem. Soc.* **2012**, *134*, 14718.
(10) Thomas, K. G.; Kamat, P. V. *Acc. Chem. Res.* **2003**, *36*, 888.
(11) Dube, H.; Ams, M. R.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2010**, *132*, 9984.
(12) Lux, J.; Rebek, J., Jr. *Chem. Commun.* **2013**, *49*, 2127.
(13) Jayaraj, N.; Zhao, Y.; Parthasarathy, A.; Porel, M.; Liu, R. S. H.; Ramamurthy, V. *Langmuir* **2009**, *25*, 10575.
(14) Gibb, C. L. D.; Gibb, B. C. *J. Am. Chem. Soc.* **2004**, *126*, 11408.
(15) Bandara, H. M. D.; Burdette, S. C. *Chem. Soc. Rev.* **2012**, *41*, 1809.
(16) Saltiel, J.; Charlton, J. L. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 3, p 25.
(17) Saltiel, J.; Sun, Y.-P. In *Photochromism: Molecules and Systems*; Durr, H., Bouas-Laurent, H., Eds.; Elsevier: Amsterdam, 1990; p 64.
(18) Lu, Y.-C.; Diau, E. W.-G.; Rau, H. *J. Phys. Chem. A* **2005**, *109*, 2090.
(19) Samanta, S. R.; Parthasarathy, A.; Ramamurthy, V. *Photochem. Photobiol. Sci.* **2012**, *11*, 1652.
(20) Hallett-Tapley, G. L.; D'Alfonso, C.; Pacioni, N. L.; McTiernan, C. D.; González-Béjar, M.; Lanzalunga, O.; Alarcon, E. I.; Scaiano, J. C. *Chem. Commun.* **2013**, *49*, 10073.
(21) Titov, E.; Lysyakova, L.; Lomadze, N.; Kabashin, A. V.; Saalfrank, P.; Santer, S. *J. Phys. Chem. C* **2015**, *119*, 17369.
(22) Yoon, J. H.; Yoon, S. *Phys. Chem. Chem. Phys.* **2011**, *13*, 12900.
(23) Simoncelli, S.; Aramendia, P. F. *Catal. Sci. Technol.* **2015**, *5*, 2110.
(24) Shin, K.-H.; Shin, E. J. *Bull. Korean Chem. Soc.* **2008**, *29*, 1259.
(25) Frens, G. *Nature, Phys. Sci.* **1973**, *241*, 20.
(26) Hohnstedt, L. F.; Miniatas, B. O.; Waller, C. M. *Anal. Chem.* **1965**, *37*, 1163.
(27) *Colloidal Gold: Principles, Methods and Applications*; Hyatt, M. A., Ed.; Academic: New York, 1989; Vol. 3.
(28) Turkevich, J.; Stevenson, P. C.; Hillier, J. A. *Discuss. Faraday Soc.* **1951**, *11*, 55.
(29) Liz-Marzan, L. M. *Langmuir* **2006**, *22*, 32.
(30) Eustis, S.; El-Sayed, M. A. *Chem. Soc. Rev.* **2006**, *35*, 209.
(31) Lewis, F. D.; Bedell, A. M.; Dykstra, R. E.; Elbert, J. E.; Gould, I. R.; Farid, S. *J. Am. Chem. Soc.* **1990**, *112*, 8055.
(32) Lewis, F. D.; Kojima, M. *J. Am. Chem. Soc.* **1988**, *110*, 8664.

DOI: 10.1021/acs.orglett.7b02963
Org. Lett. XXXX, XXX, XXX−XXX