

# Importance of Singlet Oxygen in Photocatalytic Reactions of 2-Aryl-1,2,3,4-tetrahydroisoquinolines Using Chalcogenorosamine Photocatalysts

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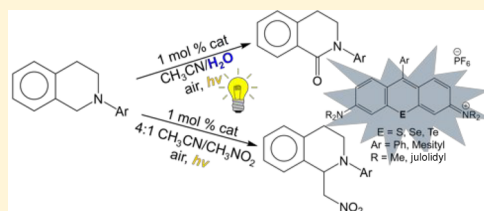
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## Supporting Information

**ABSTRACT:** Aerobic oxidation of 2-aryl-1,2,3,4-tetrahydroisoquinolines was achieved photocatalytically using chalcogenorosamine photocatalysts and LED irradiation. The photocatalytic aza-Henry reaction between these substrates and nitromethane was more efficient with selenorosamine and tellurorosamine photocatalysts than with thiorosamine and rosamine photocatalysts, corresponding to the propensity of the photocatalysts to generate singlet oxygen ( $^1\text{O}_2$ ). Appropriately, yields for the photocatalytic aza-Henry reaction were greatly reduced when the reactions were conducted under a nitrogen atmosphere. The 2-aryl-1,2,3,4-tetrahydroisoquinolines were oxidized to the corresponding 2-aryl-3,4-dihydroisoquinolones **13a–13c** with selenorosamine and tellurorosamine photocatalysts in 2% aqueous acetonitrile. Di-2-aryl-1,2,3,4-tetrahydroisoquinolin-1-yl peroxides **14a** and **14b** were shown to be intermediates in this reaction. Thiorosamine photocatalysts, which do generate  $^1\text{O}_2$  upon irradiation, did not give 2-aryl-3,4-dihydroisoquinolones. These results suggested that the exciplex between  $^1\text{O}_2$  and the chalcogen atom of the chalcogenorosamines (the corresponding pertelluroxide, perselenoxide, or persulfoxide) and/or the hydrated perchalcogenoxide [hydroxy (perhydroxy)tellurane, -selenane, or -thiane] might be an active oxidant in the formation of **13a–13c**. Computational methods were employed to provide support for the observed photocatalytic reactivity of the tellurorhodamine and selenorhodamine chromophores compared to the thiorosamine chromophores.  $\Delta G$  values were determined for the oxidation and hydration of **10-Te**, **10-Se**, and **10-S** for formation of perchalcogenoxides and hydroxyl(perhydroxy)chalcogenanes, respectively. Calculations indicate formation of the pertelluroxide perselenoxide, and persulfoxide exciplex intermediates are energetically favorable. Hydration of the exciplexes of **10-Te** and **10-Se** have similarly small  $\Delta G$  of  $-3.49$  and  $4.51$  kcal/mol, respectively. However, a significantly higher  $\Delta G$  value of  $+22.4$  kcal/mol is observed for the hydration of **10-S**, which suggests that this reactive intermediate is not readily formed.



## INTRODUCTION

Photocatalysis is a single-electron-transfer process that employs organic dyes or transition-metal complexes along with visible light irradiation.<sup>1</sup> Organic dyes have been utilized to a limited extent in photoredox catalysis, whereas ruthenium(II) and iridium(III) complexes have been extensively studied for over 30 years.<sup>2–7</sup> There are several properties of organic dyes that make them advantageous over transition-metal complexes. Organic dyes are potentially less toxic, more cost-effective, and have improved photophysical properties (increased absorption in the visible region) and high singlet oxygen yields [ $\Phi(^1\text{O}_2)$ ], making them a more practical option.<sup>5</sup>

In the past decade, photocatalysis has become of increasing interest as a “green” mode of small molecule activation within organic chemistry.<sup>8</sup> General reactions for alkylations, oxidations, and anti-Markovnikov additions to alkenes have all been developed using photocatalysis.<sup>9–12</sup> Photocatalysts employed to date have various insufficiencies. Titanium dioxide as a

photocatalyst can utilize atmospheric oxygen as an oxidant; however, it is only active in the UV region, which drastically reduces light-absorbing efficiency under solar irradiation.<sup>13</sup> Transition-metal-based Ru(II) and Ir(III) polypyridyl complexes have been more extensively studied as photocatalysts and have readily available photophysical and electrochemical properties, although these transition-metal complexes are relatively expensive.<sup>1,6,14</sup>

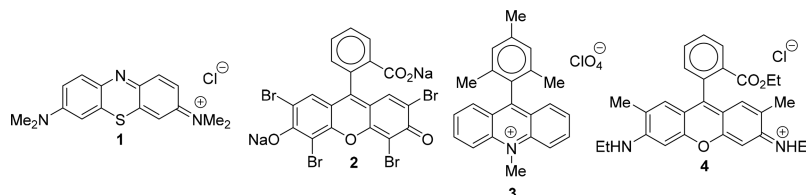
The structures of several cationic organic dyes that have been used successfully as photocatalysts are shown in Chart 1. The Scaiano group has examined methylene blue (**1**);<sup>4,15,16</sup> the König group studied eosin Y (**2**),<sup>2</sup> and various acridinium salts including the 9-mesityl derivative (**3**) were reported by the Nicewicz and Fukuzumi groups.<sup>11,12</sup> Rhodamine 6G (**4**, Chart 1) and various oxazine, thiazine, and azine dyes have been

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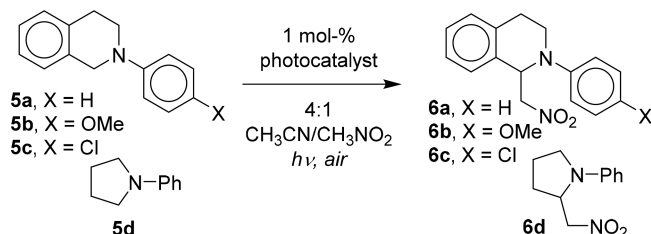
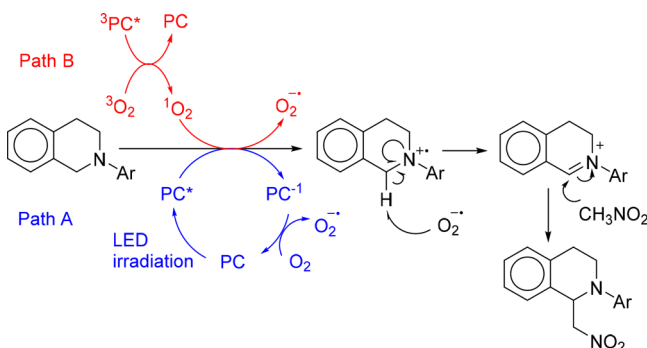
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Chart 1. Structures of Methylene Blue (1), Eosin Y (2), 9-Mesityl-10-methylacridinium (3), and Rhodamine 6G (4)



recently compared as photocatalysts for the oxidation of 2-phenyl-1,2,3,4-tetrahydroisoquinoline (**5a**) in the light-mediated aza-Henry reaction with nitromethane to give 1-nitromethyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**6a**) shown in Scheme 1.<sup>7</sup> Mechanistically, the cationic organic photocatalysts are thought to follow two different pathways (Scheme 2). Path A: the excited photocatalyst can initiate single-electron oxidations via electron transfer from a donor atom of the substrate (N in the case of **5a**) to the excited state

Scheme 1. Photocatalyzed Aza-Henry Reaction of Amine Substrates Using 1 mol % of Photocatalyst in 4:1 CH<sub>3</sub>CN/CH<sub>3</sub>NO<sub>2</sub>Scheme 2. Proposed Mechanism for the Aza-Henry Reaction<sup>a</sup>

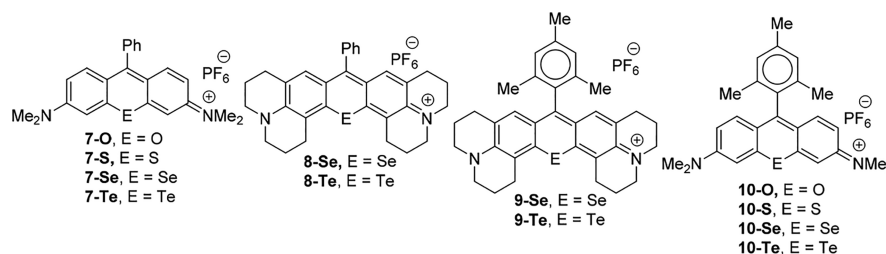
<sup>a</sup>In path A, the radical cation of the isoquinoline is formed by electron transfer from the excited photocatalyst (PC), and in path B, it is formed from electron transfer from singlet oxygen.<sup>5,7</sup>

of the photocatalyst to give a radical of the photocatalyst and a cation radical of the donor atom.<sup>5,7</sup> Alternatively, in path B, photocatalysts that produce high triplet yields can generate singlet oxygen (<sup>1</sup>O<sub>2</sub>), which oxidizes a donor atom of the substrate to give superoxide (O<sub>2</sub><sup>•-</sup>) as well as the cation radical of the donor atom.<sup>7</sup> In the light-mediated aza-Henry reaction of **5a** with nitromethane,<sup>7</sup> methylene blue (**1**) with  $\Phi(^1\text{O}_2)$  of 0.52<sup>17</sup> was a superior photocatalyst to rhodamine 6G (**4**) with  $\Phi(^1\text{O}_2)$  of 0.01.<sup>18</sup>

Chalcogenorosamine dyes 7-E–10-E (Chart 2) are similar in structure to the organic photocatalysts of Chart 1.<sup>7</sup> Whereas the chalcogenorosamines and structurally related chalcogenorhodamines have not been examined as photocatalysts in synthetic transformations of organic molecules, these molecules have been examined as photosensitizers for photoinduced charge-transfer reactions in dye-sensitized solar cells (DSSCs)<sup>19</sup> and for the generation of hydrogen via the photoreduction of protons.<sup>20</sup> The ability of the seleno- and telluororosamine/rhodamine analogues to generate <sup>1</sup>O<sub>2</sub> has been exploited in photodynamic therapy (PDT)<sup>21</sup> and in fluorescence imaging.<sup>22,23</sup>

Whereas dye chromophores incorporating O, S, Se, or Te in the heterocyclic structure generate <sup>1</sup>O<sub>2</sub>, the relative values of  $\Phi(^1\text{O}_2)$  are very much dependent on the presence of heavy atom(s). The presence of heavy atoms promotes spin–orbit coupling, which scales with nuclear charge, leading to increased rates of singlet–triplet intersystem crossing. Organic dyes incorporating the heavier chalcogen atoms Se or Te have values of  $\Phi(^1\text{O}_2)$  higher than those of their lighter chalcogen analogues because of this effect.<sup>22,24–27</sup> The Te analogues have  $\Phi(^1\text{O}_2)$  lower than that of the corresponding Se compounds likely due to reaction of <sup>1</sup>O<sub>2</sub> with the Te, resulting in lower observed <sup>1</sup>O<sub>2</sub> phosphorescence.<sup>22b</sup> Furthermore, the exciplex from <sup>1</sup>O<sub>2</sub> addition to the Te atom can undergo subsequent chemistry with water to produce H<sub>2</sub>O<sub>2</sub> and the telluroxide oxidation state (Te(IV)) of the telluororosamine.<sup>10</sup> The telluroxide, in turn, can function as an oxidant for the conversion of thiols to disulfides in a photocatalytic process.<sup>10</sup> Similar chemistry has also been observed with selenoxides, where addition of hydrogen peroxide generates the corresponding hydroxy(perhydroxy)selenane.<sup>28</sup>

Chart 2. Structures of the Chalcogenorosamines 7-E (E = O, S, Se, Te), 8-E (E = Se, Te), 9-Te, and 10-E (E = O, S, Se, Te)

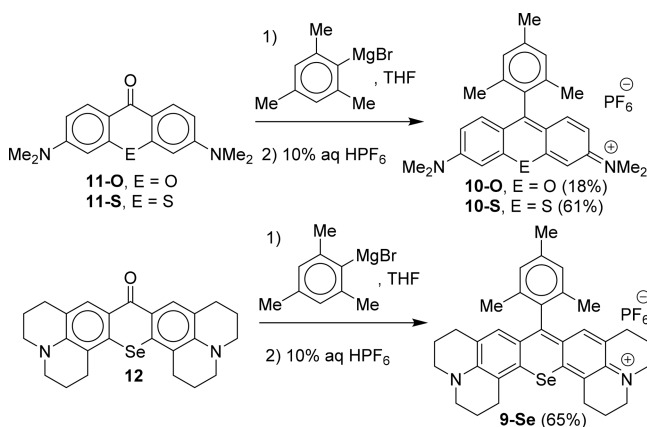


Herein, we compare the chalcogenorosamines 7-E–10-E (Chart 2) as photocatalysts for two reactions of 2-aryl-1,2,3,4-tetrahydroisoquinolines: (1) the aza-Henry reaction with nitromethane to give 1-nitromethyl-2-aryl-1,2,3,4-tetrahydroisoquinolines and (2) the oxidation to the corresponding 2-aryl-3,4-dihydroisoquinolones. The latter reaction is a new photocatalytic reaction, and the importance of the singlet oxygen–photocatalyst exciplex (pertelluroxide, perselenoxide, or persulfoxide) in this process was examined using density functional theory (DFT) calculations. Isoquinolones are of interest due their prevalence in alkaloidal natural products. We have chosen the substrates to allow for direct comparison to previous photocatalytic reactions.<sup>7</sup>

## RESULTS AND DISCUSSION

**Chalcogenorosamine Photosensitizers.** The tetramethylchalcogenorosamine 7-E,<sup>24,25,29</sup> bisjulolidylchalcogenorosamine 8-E,<sup>22b</sup> and the respective 9-mesityl derivatives 9-Te<sup>22b</sup> and 10-E (E = Se, Te)<sup>10,22a</sup> were prepared as previously described. The lighter chalcogen analogues 10-O and 10-S and bisjulolidylselenorosamine 9-Se were prepared as shown in Scheme 3.<sup>22b</sup> Values of absorption maxima ( $\lambda_{\text{max}}$ )

**Scheme 3.** Synthesis of 9-Mesitylselenorosamine 10-O, 9-Mesitylthiorosamine 10-S, and 9-Mesitylselenorosamine 9-Se



and extinction coefficients ( $\epsilon$ ) for 9-Se, 10-O, and 10-S are compiled in Table 1. In order to compare complete sets of photophysical properties among the rosamine series 7-E and 10-E, steady-state fluorescence spectra for 10-O and 10-S were acquired as were values of  $\Phi(^1\text{O}_2)$  (Table 1). Emission maxima ( $\lambda_{\text{FL}}$ ) in MeOH were 572 nm for 10-O and 598 nm for 10-S. Quantum yields for fluorescence ( $\Phi_{\text{FL}}$ ) in MeOH were  $0.74 \pm 0.04$  for 10-O and  $0.34 \pm 0.2$  for 10-S. Values of  $\Phi(^1\text{O}_2)$  were measured using time-resolved spectroscopy of  $^1\text{O}_2$  phosphorescence in air-saturated methanol with 7-Se as a reference [ $\Phi(^1\text{O}_2) = 0.87$ ].<sup>25,30–32</sup> Values of  $\Phi(^1\text{O}_2)$  were  $0.03 \pm 0.01$  for 10-O and  $0.61 \pm 0.02$  for 10-S.

**2-Aryl-1,2,3,4-tetrahydroisoquinolines.** The 2-aryl-1,2,3,4-tetrahydroisoquinolines used in this study were prepared as shown in Scheme 4.<sup>5</sup> 1,2,3,4-Tetrahydroisoquinoline was coupled to an aryl iodide using CuI as catalyst. 2-Phenyl-1,2,3,4-tetrahydroisoquinoline (5a) was isolated in 70% yield, the 2-(4-methoxyphenyl) derivative 5b in 39% yield, and the 2-(4-chlorophenyl) derivative 5c in 78% yield.

**Photocatalyzed Aza-Henry Reaction of 5a.** The photocatalyzed aza-Henry reaction of 5 with nitromethane, as shown in Scheme 1, was evaluated using 1 mol % of each of the chalcogenorosamines of Chart 2 and compared to methylene blue (1) and rhodamine 6G (4) as controls. A 4:1  $\text{CH}_3\text{CN}/\text{CH}_3\text{NO}_2$  solution of 5a (0.06 M) and photocatalyst (0.0006 M) was irradiated for 3.0 h with a GE 14 W, 850 lm LED light. The % conversion of 5a to 6a was determined by  $^1\text{H}$  NMR spectroscopy comparing the integral of the 2-nitromethyl methylene protons ( $\delta$  4.81 and 4.53) and the 1-methine proton ( $\delta$  5.51) of 6a with the 1-methylene protons ( $\delta$  4.42) of 5a. Values of % conversion are compiled in Table 1 and are the mean of triplicate runs.

Both tetramethyltellurorosamine 7-Te and 9-phenyl bisjulolidyltellurorosamine 8-Te bleached rapidly and gave <1% conversion of 5a to the aza-Henry product 6a. The three xanthylum core photocatalysts 4 (rhodamine 6G), 7-O, and 10-O gave  $\leq 18\%$  conversion of 5a to 6a and were not significantly different from one another (probability value,  $p > 0.10$ , one-way ANOVA). Photocatalysts 4, 7-O, 7-Te, 8-Te, and 10-O were all significantly poorer photocatalysts ( $p \leq 0.0064$ , one-way ANOVA) than the remaining catalysts of Table 1. Selenorosamines 7-Se, 8-Se, and 10-Se and tellurorosamine 10-Te were the best photocatalysts for conversion of 5a to 6a after 3 h, collectively, with  $\geq 94\%$  conversion of 5a to 6a.

Conversions of 5a to 6a were also run for 1.0 h with the best performing photocatalysts 7-Se, 8-Se, 10-Se, and 10-Te in aerated solvent. Values of % conversion are compiled in Table 1 and are the mean of triplicate runs. The 60% conversion with 7-Se as photocatalyst and 56% conversion with 10-Te as photocatalyst were not significantly different ( $p > 0.10$ , one-way ANOVA) from one another. However, the 1 h conversion with both of these catalysts was significantly greater ( $p \leq 0.03$ ) than the 1 h conversion with 8-Se (37%) and 10-Se (45%), which were not significantly different from one another ( $p > 0.07$ ). However, for all four of these photocatalysts, greater conversions were observed with longer reaction times.

In order to assess the importance of oxygen in the photocatalyzed reactions, the reactions were repeated with several of the photocatalysts following deaeration with  $\text{N}_2$  bubbling to remove most of the oxygen from the reaction vessel. Values of % conversion under a  $\text{N}_2$  atmosphere with irradiation for 3 h are compiled in Table 1 and are the mean of triplicate runs. In every example, product yields were reduced under a  $\text{N}_2$  atmosphere. The non-negligible yields (10–14%) did not increase over time and are attributed to residual oxygen (Table 1).

**Preparative Photocatalyzed Aza-Henry Reactions.** The survey of chalcogenorosamine photocatalysts suggested that 7-Se and 10-Te were perhaps the two most robust and efficient among the photocatalysts compared in Table 1 for the aza-Henry reaction. The aza-Henry reaction was repeated on a 1.0 mmol scale with 1 mol % of photocatalyst (either 7-Se or 10-Te), nitromethane, and tetrahydroisoquinoline substrates 5a, 5b, and 5c (Scheme 1 and Table 2). Reactions were followed by thin layer chromatography (TLC) until consumption of starting amine was complete. Following irradiation with the LED light, reaction mixtures were concentrated and the product(s) were isolated via chromatography on  $\text{SiO}_2$  eluted with 5% EtOAc in hexanes.

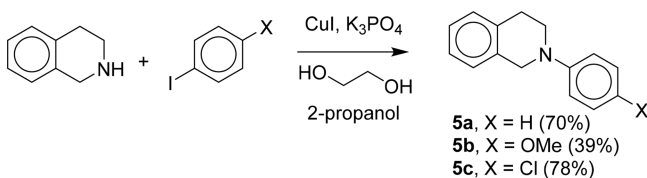
The photocatalyzed aza-Henry reaction of *N*-phenylpyrrolidine (5d) with nitromethane and 1 mol % of 7-Se or 10-Te

Table 1. Comparison of Photocatalysts for the Photocatalyzed Aza-Henry Reaction of 5a with Nitromethane To Give 6a

photocatalyst	$\lambda_{\text{max}}$ , nm	$\epsilon$ , M <sup>-1</sup> cm <sup>-1</sup>	% conversion <sup>a</sup>			$\Phi(^1\text{O}_2)$
			3.0 h	N <sub>2</sub> , 3.0 h	1.0 h	
1	664 <sup>b</sup>	90000 <sup>b</sup>	42 ± 3	<1		0.52 <sup>c</sup>
4	524 <sup>b</sup>	78000 <sup>b</sup>	18 ± 3	<1		0.01 <sup>d</sup>
7-O	536	108000	18 ± 5	<1		0.08 <sup>e</sup>
7-S	557	94400	69 ± 8	9 ± 4		0.21 <sup>e</sup>
7-Se	568	117000	94 ± 2	14 ± 2	60 ± 1	0.87 <sup>e</sup>
7-Te	601 <sup>f</sup>	81000 <sup>f</sup>	<1			0.43 <sup>g</sup>
8-Se	604 <sup>h</sup>	135000 <sup>h</sup>	98 ± 1	10 ± 2	37 ± 4	0.68 <sup>h</sup>
8-Te	617 <sup>h</sup>	144000 <sup>h</sup>	<1			0.53 <sup>h</sup>
9-Se	604	145000	60 ± 6			
9-Te	617 <sup>h</sup>	165000 <sup>h</sup>	80 ± 20			
10-O	537	124000	12 ± 4			0.03 ± 0.01
10-S	557	124000	44 ± 7			0.61 ± 0.02
10-Se	568 <sup>i</sup>	103000 <sup>i</sup>	99.5 ± 0.5	16 ± 2	45 ± 4	0.85 <sup>i</sup>
10-Te	600 <sup>g</sup>	86000 <sup>g</sup>	95 ± 1	14 ± 1	56 ± 3	0.75 <sup>g</sup>

<sup>a</sup>Reagents and photocatalyst were dissolved in a 4:1 mixture of MeCN/MeNO<sub>2</sub> on a 0.3 mmol scale, and the resulting solution was then irradiated with a GE 14 W, 850 nm LED light with stirring for the indicated time period. Percent conversions were determined by <sup>1</sup>H NMR spectroscopy. Values represent the mean of triplicate runs ± 1 SD. <sup>b</sup>From ref 7. <sup>c</sup>From ref 18. <sup>d</sup>From ref 19. <sup>e</sup>From ref 24. <sup>f</sup>From ref 28. <sup>g</sup>From ref 22a. <sup>h</sup>From ref 22b. <sup>i</sup>From ref 10.

**Scheme 4. Coupling of Aryliodides to 1,2,3,4-Tetrahydroisoquinoline To Give 2-Aryl-1,2,3,4-tetrahydroisoquinolines 5a, 5b, and 5c**



**Table 2. Photochemical Aza-Henry Reaction of 1.0 mmol 2-Aryl-1,2,3,4-tetrahydroisoquinolines 5a, 5b, and 5c and N-Phenylpyrrolidine 5d in 4:1 CH<sub>3</sub>CN/CH<sub>3</sub>NO<sub>2</sub> with 1 mol % of Photocatalyst 7-Se or 10-Te and LED Irradiation**

entry	photocatalyst	substrate	$h\nu$ , h	product	isolated yield, %
1	7-Se	5a	11	6a	84 <sup>a</sup>
2	10-Te	5a	5	6a	85 <sup>b</sup>
3	7-Se	5b	8.5	6b	81 <sup>c</sup>
4	10-Te	5b	6.5	6b	75 <sup>d</sup>
5	7-Se	5c	5	6c	62 <sup>e</sup>
6	10-Te	5c	4	6c	85 <sup>f</sup>
7	7-Se	5d	30	6d	3
8	10-Te	5d	30	6d	6

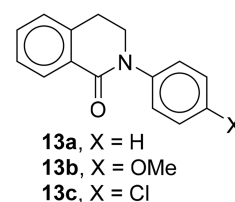
<sup>a</sup>Isoquinolone 13a isolated in 16% yield. <sup>b</sup>Isoquinolone 13a formed in trace (<2%) amounts. <sup>c</sup>Isoquinolone 13b isolated in 2% yield. <sup>d</sup>Isoquinolone 13b formed in trace (<2%) amounts. <sup>e</sup>Isoquinolone 13c isolated in 17% yield. <sup>f</sup>Isoquinolone 13c formed in trace (<2%) amounts.

was also examined. The reaction with 5d was only partially complete with either photocatalyst after 48 h of irradiation with the LED light and is consistent with previous results with this substrate and other organo photocatalysts.<sup>5</sup> Following chromatography on SiO<sub>2</sub> eluted with 5% EtOAc/hexanes, the aza-Henry product 6d was isolated in roughly 3% yield with 7-Se as the photocatalyst and in roughly 6% yield with 10-Te as the photocatalyst (Table 2).

2-Aryl-1,2,3,4-tetrahydroisoquinolines also gave various amounts of the corresponding 2-aryl-3,4-dihydroisoquinolones

13a–13c<sup>33</sup> (Chart 3) as minor products in the photocatalyzed aza-Henry reaction, as compiled in Table 2. These materials were isolated via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes.

**Chart 3. Isoquinolone Products Formed during the Photocatalyzed Aza-Henry Reaction**



**Oxidation of 1,2,3,4-Tetrahydroisoquinolines to 3,4-Dihydroisoquinolones.** There are relatively few methods for oxidizing tetrahydroisoquinolines to the corresponding dihydroisoquinolones, and the most successful example using relay aerobic oxidation required an oxygen atmosphere and Schlenk line techniques and was limited to 0.25 mmol in scale.<sup>33</sup> For most examples of oxidation of benzylic amines to benzylic amides, the amides were isolated as a minor product of the reaction,<sup>34</sup> which is what was observed in the preparative aza-Henry reactions described above to give the dihydroisoquinolones as minor products. We sought conditions to form the dihydroisoquinolones as the major product of photocatalysis. Running the photo-oxidations in pure CH<sub>3</sub>CN or CH<sub>2</sub>Cl<sub>2</sub> with 7-S, 7-Se, 10-S, 10-Se, and 10-Te as photocatalysts gave little if any dihydroisoquinolone. However, addition of 2% water to CH<sub>3</sub>CN gave photo-oxidation of the tetrahydroisoquinolines to the corresponding dihydroisoquinolones as the major product upon LED irradiation with 7-Se, 10-Se, and 10-Te, indicating that water was a necessary component of the reaction.

Photo-oxidation of 5a, 5b, and 5c was carried out on a 1.0 mmol preparative scale with 1 mol % of chalcogenorosamine photocatalysts 7-S, 7-Se, 10-S, 10-Se, or 10-Te using a 4.9:0.1 solution of CH<sub>3</sub>CN/H<sub>2</sub>O as solvent under irradiation with an



850 nm LED light. The reactions were followed by TLC until the consumption of the starting tetrahydroisoquinoline was complete. Using 7-Se (entries 2, 3, 7, 11, and 12), 10-Se (entries 4, 9, 13, and 14), or 10-Te (entries 5, 10, and 15) as the photocatalyst, the known 2-aryl-3,4-dihydroisoquinolin-1(2H)-ones 13a–c<sup>33</sup> were isolated as the major products of reaction, as shown in Table 3. Irradiating 1,2,3,4-tetrahydro-

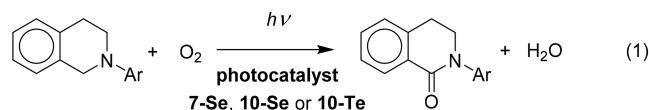
**Table 3. Photochemical Oxidation of 1.0 mmol 2-Aryl-1,2,3,4-tetrahydroisoquinolines 5a, 5b, and 5c in 4.9:0.1 CH<sub>3</sub>CN/H<sub>2</sub>O with 1 mol % of Photocatalyst and LED Irradiation**

entry	photocatalyst	substrate	hν, h	product	isolated yield, %
1	7-S	5a	12	13a	<5
2	7-Se	5a	8	13a	58
3	10-S	5a	12	13a	<5
4	10-Se	5a	8	13a	83
5	10-Te	5a	8	13a	63
6	7-S	5a	12	13a	<5
7	7-Se	5b	13	13b	63
8	10-S	5b	12	13b	<5
9	10-Se	5b	13	13b	73
10	10-Te	5b	8	13b	75
11	7-Se	5c	7.5	13c	78 <sup>a</sup>
12	7-Se	5c	36	13c	89
13	10-Se	5c	8	13c	70 <sup>b</sup>
14	10-Se	5c	36	13c	85
15	10-Te	5c	3	13c	59

<sup>a</sup>Peroxodimer 14a isolated in 6% yield. <sup>b</sup>Peroxodimer 14a isolated in 12% yield.

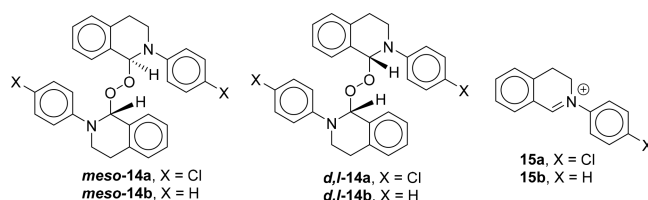
dihydroisoquinoline 5a or 5b for 12 h using thiorosamine photocatalysts 7-S (entries 1 and 6) and 10-S (entries 3 and 8) gave essentially unreacted 5a or 5b and no isolable amounts of 13a or 13b or other products.

The importance of oxygen in the photocatalysis was demonstrated by reducing the oxygen content of the reaction mixture prior to irradiation. Irradiating 1,2,3,4-tetrahydroisoquinoline 5a and photocatalyst 7-Se or 10-Te in a 4.9:0.1 solution of CH<sub>3</sub>CN/H<sub>2</sub>O as solvent that had been deaerated with a stream of N<sub>2</sub> gas and then placed under a N<sub>2</sub> atmosphere returned unreacted 5a. Isoquinolone 13a was not observed. The photocatalytic conversion of the tetrahydroisoquinolines to the dihydroisoquinolones is summarized in eq 1. Oxygen as it is found in air is the reagent, and water is the byproduct of the photocatalytic oxidation reaction, providing an environmentally benign approach to the synthesis.



**Oxidized Peroxo Intermediate.** During the photo-oxidation of 5c with photocatalyst 7-Se in a 4.9:0.1 solution of CH<sub>3</sub>CN/H<sub>2</sub>O, a white precipitate formed and, when consumption of 5c was complete, was isolated by filtration. The solid was identified as a mixture of the *meso*- and *D,L*-diastereomers of the peroxodimer 14a (Chart 4) primarily through NMR spectral data (Supporting Information) and elemental analysis. The mass spectrum of the white solid gave *m/z* 242 as the parent ion with no higher mass peaks, which is consistent with iminium ion 15a (C<sub>15</sub>H<sub>13</sub><sup>35</sup>ClN<sup>+</sup>). However,

**Chart 4. *meso*- and *D,L*-Diastereomers of Peroxodimers 14a and 14b and the Structure of Iminium Ions 15a and 15b**



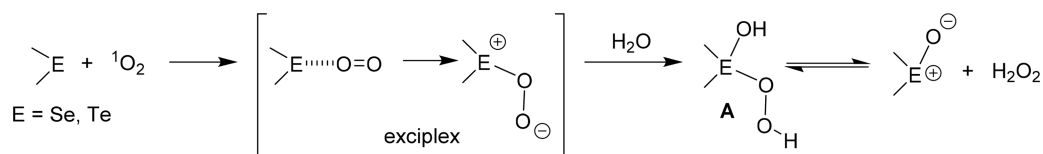
the <sup>1</sup>H NMR spectrum of the mixture of diastereomers of 14a indicated that the pairs of methylene protons at C3 and C4 were no longer equivalent and geminal coupling was observed. Two singlets were observed in a ratio of 45:55 at δ 6.09 and δ 5.98 for a methine proton at C1, which suggested two compounds were produced in not quite a 1:1 ratio. Combustion analysis was consistent with a dimer of the iminium core perhaps bridged by two oxygen atoms with calculated element percentages for C<sub>30</sub>H<sub>26</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub> of C, 69.64; H, 5.06; and N, 5.41. Experimentally determined percentages were C, 69.98; H, 4.92; and N, 5.41.

The <sup>13</sup>C{<sup>1</sup>H} NMR spectrum of the mixture of diastereomers of 14a was also consistent with a nearly 1:1 mixture of the *meso*- and *D,L*-diastereomers. Each diastereomer would have 30 carbons with two identical halves. The symmetry of the 4-chlorophenyl substituent in each would reduce the number of different carbon signals to 26 for each diastereomer, with the mirror plane and C<sub>2</sub> axis reducing the number of unique signals to 13 for each diastereomer or 26 signals in total. The experimental <sup>13</sup>C{<sup>1</sup>H} NMR spectrum displayed 21 unique signals for the mixture with the “overlapped” signals observed at δ 136.0, 128.2, 125.7, 115.7, and 42.2. The remaining signals were “paired” with very similar chemical shifts (Supporting Information).

The white precipitate of 14a began forming when irradiation began and the quantity of precipitate reached a maximum and began declining as irradiation continued. When irradiation was stopped after 4 h (rather than 7.5 h), the white precipitate of 14a was isolated in 13% yield. After 7.5 h, consumption of 5c was complete and the precipitate was isolated in 6% yield. The precipitate of 14a disappeared after 36 h of irradiation, and isoquinolone 13c was isolated in 89% yield at this point. If the precipitate were returned to a fresh 4.9:0.1 solution of CH<sub>3</sub>CN/H<sub>2</sub>O (no photocatalyst or 13c) and LED irradiation continued, isoquinolone 13c was formed along with other products, which were not identified.

Similar products were observed in the photo-oxidation of 5a using 7-Se or 10-Te as photocatalyst with LED irradiation in 4.9:0.1 CH<sub>3</sub>CN/H<sub>2</sub>O. The <sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} NMR spectra for the mixture of the *meso*- and *D,L*-peroxodimer 14b were strikingly similar to those for the mixture of the *meso*- and *D,L*-peroxodimer 14a (Supporting Information). After 3 h of LED irradiation with photocatalyst 10-Te, photo-oxidation of 2-phenyl-1,2,3,4-tetrahydroisoquinoline 5a in 4.9:0.1 CH<sub>3</sub>CN/H<sub>2</sub>O as solvent was complete—5a was no longer observed in the reaction mixture by TLC. At this point, a 9:1 mixture of the *meso*- and *D,L*-peroxodimer 14b to the isoquinolone 13a was formed (Figure S1, Supporting Information). Further LED irradiation for an additional 5 h gave complete disappearance of the *meso*- and *D,L*-peroxodimer 14b, and isoquinolone 13a was isolated in 63% yield from the reaction mixture.

**Scheme 5.** Formation of Hydroxy(perhydroxy)tellurane (E = Te) or Hydroxy(perhydroxy)selenane (E = Se) Intermediate upon Addition of Water to the Chalcogenide–Singlet Oxygen Exciplex (Pertelluroxide or Perselenoxide Intermediate)



The reaction mixture obtained after 3 h of LED irradiation was purified via chromatography on  $\text{SiO}_2$ , and a band containing mostly a mixture of *meso*- and *D,L*-**14b** was isolated as a colorless oil. The mass spectrum of the colorless oil gave  $m/z$  208 as the parent ion with no higher mass peaks, which is consistent with iminium ion **15b** ( $\text{C}_{15}\text{H}_{14}\text{N}^+$ ). The NMR spectral data for *meso*- and *D,L*-**14b** was strikingly similar to that of *meso*- and *D,L*-**14a** (Supporting Information). The  $^1\text{H}$  NMR spectrum of the mixture showed that the pairs of methylene protons at C3 and C4 were no longer equivalent, and geminal coupling was observed. Two singlets were observed in a ratio of 45:55 at  $\delta$  6.09 and  $\delta$  5.98 for a methine proton at C1, which suggested two compounds were produced in not quite a 1:1 ratio. The mixture of *meso*- and *D,L*-**14b** was not stable and decomposed to many products upon standing overnight under ambient conditions or at  $-20^\circ\text{C}$  under a nitrogen atmosphere. Again, for the *meso*- and *D,L*-**14a**, a total of 26 unique signals would be expected in the carbon NMR, and 21 of the expected 26 signals were observed with the “overlapped” carbons appearing at  $\delta$  136.0, 128.2, 127.3, 115.7, and 42.2 (Supporting Information).

**Mechanistic Implications with Chalcogenorosamine Photocatalysts.** *a. Importance of Singlet Oxygen.* The presence of oxygen and, in particular, the generation of  ${}^1\text{O}_2$  appear to be important both for the photochemical aza-Henry reaction and for the photo-oxidation of the tetrahydroisoquinolines to the dihydroisoquinolones. The importance of  ${}^1\text{O}_2$  in the aza-Henry reaction has been well-documented, with  ${}^1\text{O}_2$  accepting an electron from the donor atom (in this case, the N of the tetrahydroisoquinoline) to generate superoxide ( $\text{O}_2^{\bullet-}$ ) as well as the cation radical of the donor atom.<sup>5,7</sup> Alternatively, the excited-state photosensitizer can induce single-electron transfer from the donor atom.

The results compiled in Table 1 show that photocatalysts with higher values of  $\Phi({}^1\text{O}_2)$  give greater conversions of 1,2,3,4-tetrahydroisoquinoline **5a** to aza-Henry product **6a**. The exceptions are tellurorosamine catalysts **7-Te** and **8-Te**, with phenyl substituents in the 9-position that do not shield the 9-position from nucleophilic addition.<sup>35</sup> The selenorosamines **7-Se** and **8-Se** and Se- and Te-containing photocatalysts with a 9-mesityl substituent **9-Se**, **9-Te**, **10-Se**, and **10-Te** have much greater stability and gave higher conversions of **5a** to **6a** than methylene blue (**1**), rhodamine **6G** (**4**), rosamines **7-O** and **10-O**, thiorosamines **7-S** and **10-S**, and tellurorosamines **7-Te** and **8-Te**. These results also reflect relative values of  $\Phi({}^1\text{O}_2)$ .

When the reaction mixtures were deaerated with a stream of  $\text{N}_2$  gas prior to irradiation in the aza-Henry reaction, overall conversion of **5a** to **6a** was greatly reduced (Table 1), indicating the importance of  ${}^1\text{O}_2$  in the photocatalyzed aza-Henry reaction with this set of photocatalysts. The absence of formation of isoquinolone **13a** upon photo-oxidation of **5a** with photocatalyst **7-Se** or **10-Te** in deaerated 4.9:0.1  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$  also indicates the importance of oxygen and,

specifically,  ${}^1\text{O}_2$  in the photo-oxidation of the tetrahydroisoquinolines to the dihydroisoquinolones.

*b. Importance of Water and the Chalcogenorosamine- ${}^1\text{O}_2$  Exciplex in the Photocatalytic Oxidation to the Dihydroisoquinolones.* In the absence of water, the oxidation of tetrahydroisoquinolines to dihydroisoquinolones is not observed with 1 mol % of photocatalyst, LED irradiation, and pure  $\text{CH}_2\text{Cl}_2$  or  $\text{CH}_3\text{CN}$  as solvent. However, the addition of 2% water to  $\text{CH}_3\text{CN}$  gives oxidation of the tetrahydroisoquinolines to the dihydroisoquinolones with selenorosamine and tellurorosamine photocatalysts as compiled in Table 3. The addition of water to the exciplex between  ${}^1\text{O}_2$  and diorganotellurides and diorganoselenides (a pertelluroxide or perselenoxide intermediate) has a rich chemistry, as shown in Scheme 5, to give the corresponding hydroxy(perhydroxy)-tellurane<sup>10</sup> or hydroxy(perhydroxy)selenane<sup>28</sup> (intermediate **A** in Scheme 5). Intermediates **A** can function as an oxidant or they can eliminate  $\text{H}_2\text{O}_2$  to generate the corresponding selenoxide or telluroxide.<sup>10</sup> The telluroxide can be reduced back to the starting catalyst in a Swern-like oxidation, transforming the 1,2,3,4-tetrahydroisoquinoline to 3,4-dihydroisoquinolone (Supporting Information).

*c. Enigma of the Thiorosamine Photocatalysts 7-S and 10-S.* The other interesting feature of the photo-oxidation to the dihydroisoquinolones is that the thiorosamine photocatalysts **7-S** and **10-S** do not give isolable amounts of dihydroisoquinolones as a product of the reaction after 12 h of irradiation in 4.9:0.1  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ . Both of these photocatalysts generate  ${}^1\text{O}_2$  upon irradiation with values of  $\Phi({}^1\text{O}_2)$  of 0.21 for **7-S** and 0.61 for **10-S** (Table 1). If  ${}^1\text{O}_2$  alone were responsible for oxidation to the tetrahydroisoquinoline to the isoquinolone, one would reasonably expect some oxidation to be observed. Because no oxidation was observed, one might examine the differences in the chalcogenorosamine photocatalysts upon generating  ${}^1\text{O}_2$ . The other key feature of the photo-oxidation reactions is the necessity of having water as part of the solvent system.

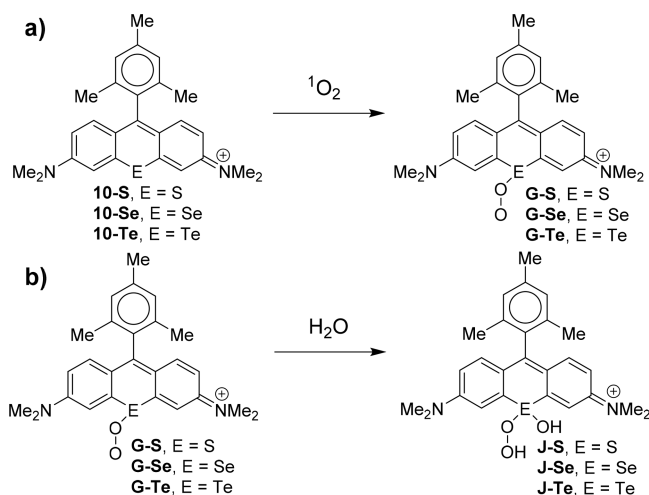
Photocatalysis with the 3-aryl-1,2,3,4-tetrahydroisoquinolines has been shown to proceed through single-electron oxidation of the 3-aryl-1,2,3,4-tetrahydroisoquinoline and subsequent loss of a hydrogen atom to give the corresponding iminium compound (structures **15a** and **15b** in Chart 4, as examples). Both **7-S** and **10-S** are capable of generating the intermediate iminium compound as both of these photocatalysts form product in the aza-Henry reaction (Table 1). However, the hydroxy(perhydroxy)thiane intermediate corresponding to **A** in Scheme 5 has not been implicated in reactions of sulfoxides with hydrogen peroxide.<sup>28</sup>

We repeated the photo-oxidation of **5** with thiorosamine **10-S** as the photocatalyst in 4.9:0.1  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ , with 8.8 M aqueous  $\text{H}_2\text{O}_2$  replacing water to give a 4.9:0.1  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$  mixture that was 0.18 M in  $\text{H}_2\text{O}_2$ . After 8 h of irradiation with the LED, tetrahydroisoquinoline **5a** had been consumed and a 1:9 mixture dihydroisoquinolone **13a** and peroxodimers **14b**

was observed by  $^1\text{H}$  NMR spectroscopy in the reaction mixture (Figure S2, Supporting Information). These results strongly suggest that either  $\text{H}_2\text{O}_2$  or the hydroxy(perhydroxy)-chalcogenane intermediate **A** in Scheme 5 is responsible for oxidation of the iminium ion intermediates in the photo-oxidation of the tetrahydroisoquinolines to the dihydroisoquinolones. As only 1 equiv of  $\text{H}_2\text{O}_2$  can be produced from each oxidation, the high yields implicate oxidation by intermediate **A** that would regenerate the catalyst. We next examined the energetics of formation of the  $^1\text{O}_2$ -chalcogenorosanamine exciplex (the corresponding pertelluroxide, perselenoxide, or persulfoxide intermediate) and its addition product with  $\text{H}_2\text{O}$ .

**DFT Calculations.** Computational methods were employed to provide support for the observed photocatalytic reactivity of the tellurorhodamine and selenorhodamine chromophores compared to the thiorosamine chromophores. All structures were optimized using the Gaussian09 software package<sup>36</sup> at the B3LYP level of theory.<sup>37–39</sup> The geometries of **10-Se** and **10-S** were optimized using a 6-31+G(d) basis set.<sup>40–42</sup> A split basis set was used for **10-Te** (Lan12DZ<sup>43–45</sup> for the tellurium atom and 6-31+G(d) for all other atoms).<sup>46</sup> All geometries were optimized in  $\text{CH}_3\text{CN}$  using the SMD solvation model.<sup>47</sup> Energy values were obtained from the frequency calculations of the optimized geometries and used to determine the Gibbs free energies of the reactions ( $\Delta G$ ).  $\Delta G$  values were determined for the oxidation and hydration of diorganochalcogenides **10-Te**, **10-Se**, and **10-S**, as shown in Scheme 5. The balanced equations used to determine the  $\Delta G$  values are shown in Scheme 6. All calculated values for  $\Delta G$  are summarized in Table 4.

**Scheme 6.** Balanced Equations for (a) Formation of the Exciplex from **10-E** via Reaction with  $^1\text{O}_2$  and (b) Hydration of the Exciplexes To Form the (Perhydroxy)hydroxychalcogen Species

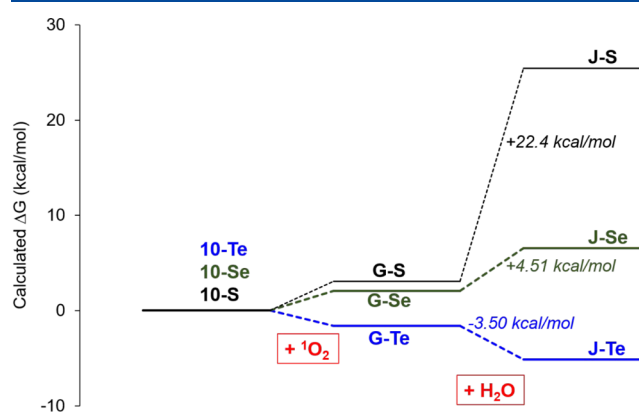


The energy of formation of the  $^1\text{O}_2$ -bound exciplex was explored first to investigate the reactivity of **10-Se** and **10-Te** relative to that of **10-S** as photocatalysts. Although **10-Te** has the lowest energy of formation of **G-Te** at  $-1.67$  kcal/mol, the calculated  $\Delta G$  values for **G-Se** and **G-S** have small positive values, 2.06 and 3.08 kcal/mol. Thus exciplex formation occurs with minimal change in  $\Delta G$  for **10-Te**, **10-Se**, and **10-S** and would not explain the difference in reactivity. Hydration of the exciplexes of **10-Te** and **10-Se** have similarly small  $\Delta G$ , with

**Table 4.** Calculated  $\Delta G$  Values for the Formation of **G-E** and **J-E** ( $\text{E} = \text{Te, Se, S}$ )

compound	calculated $\Delta G$ of formation (kcal/mol)
<b>G-Te</b>	$-1.62$
<b>G-Se</b>	$2.06$
<b>G-S</b>	$3.08$
<b>J-Te</b>	$-3.49$
<b>J-Se</b>	$4.51$
<b>J-S</b>	$22.35$

$-3.49$  kcal/mol for **G-Te** and  $4.51$  kcal/mol for **G-Se**. However, a significantly higher  $\Delta G$  of  $+22.4$  kcal/mol is observed for the hydration of **G-S**, which suggests that the reactive intermediate **J-S** is not readily formed. This is consistent with both the lack of dihydroisoquinolone formation with thiorosamine photocatalysts as well as the requirement of water in the reaction. A summary of the calculated  $\Delta G$  values for each reaction can be visualized in the reaction coordinate diagram in Figure 1.



**Figure 1.** Reaction coordinate diagram of oxidation and hydration of chalcogenorosanamine photocatalysts in Scheme 6. Energies are relative to **10-Te**, **10-Se**, and **10-S** and follow from Scheme 5.

Seferos and co-workers proposed the  $\text{Te(VI)}$ dioxo intermediate for tellurophene derivatives;<sup>49</sup> however, under the oxidation conditions of this study, this intermediate is unlikely to be observed, although this intermediate can be minimized computationally. Other oxidative addition products, such as a telluradioxirane with a three-membered ring with  $\text{O}_2$  and the chalcogen atom as proposed previously,<sup>27</sup> were studied by DFT calculations. However, for **10-Te**, the three-membered ring opened when optimized to the pertelluroxide intermediate proposed in the paper.

## CONCLUSIONS

The seleno- and tellurorosanamines bring very high quantum yields for the generation of singlet oxygen to photocatalysts used in organo photocatalysis. In well-studied reactions, such as the photochemical aza-Henry reaction with 2-aryl-1,2,3,4-tetrahydroisoquinolines,<sup>5–7</sup> the higher values of  $\Phi(^1\text{O}_2)$  for **7-Se**, **10-Se**, and **10-Te** lead to higher photochemical conversions to product. With other substrates, the transient formation of the chalcogen–singlet oxygen exciplex (the corresponding pertelluroxide or perselenoxide intermediate) can lead to oxidation chemistry not observed with other organic photocatalysts. The oxidation of 2-aryl-1,2,3,4-tetrahydroisoquinolines to 2-aryl-3,4-dihydroisoquinolones



proceeds via formation of a peroxo dimer, which is formed from the oxidized photocatalyst.

## EXPERIMENTAL SECTION

**Preparation of 9-(2,4,6-Trimethylphenyl)bisjulolidyl-selenosamine Hexafluorophosphate (9-Se).** 2-Bromomesitylene (0.663 g, 0.510 mL, 3.33 mmol) was added to a stirred suspension of magnesium turnings (0.088 g, 3.7 mmol) in dry THF (2 mL) under a dry N<sub>2</sub> atmosphere. The mixture was stirred at ambient temperature for 1 h, and the resulting solution of Grignard reagent was transferred via cannula to a stirred suspension of bisjulolidylselenoxanthone 12<sup>22b</sup> (0.100 g, 0.222 mmol) in dry THF (7 mL). The resulting solution was heated at reflux for 16 h, cooled to ambient temperature, and then poured into 25 mL of 10% (by weight) aqueous HPF<sub>6</sub>. The aqueous mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 25 mL), and the combined organic extracts were washed with brine, dried over MgSO<sub>4</sub>, and concentrated. The residue was recrystallized from 9:1 CH<sub>3</sub>CN/diethyl ether to give 0.101 g (65%) of the desired product as a green solid, mp 240–241 °C: <sup>1</sup>H NMR (500 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.05 (s, 2 H), 6.95 (s, 2 H), 3.55–3.42 (m, 8 H), 2.86 (t, 4 H, J = 6.0 Hz), 2.63 (t, 4 H, J = 6.0 Hz), 2.43 (s, 3 H), 2.18 (quint, 4 H, J = 5.0 Hz), 1.94 (quint, 4 H, J = 5.0 Hz), 1.81 (s, 6 H); <sup>13</sup>C{<sup>1</sup>H} NMR (75.5 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 161.1, 150.1, 142.5, 140.6, 136.6, 136.0, 134.9, 130.4, 126.9, 120.3, 118.1, 53.1, 52.2, 29.6, 27.8, 22.9, 22.4, 22.2, 21.3; λ<sub>max</sub> (CH<sub>2</sub>Cl<sub>2</sub>) 590 nm (ε = 1.31 × 10<sup>5</sup> M<sup>-1</sup> cm<sup>-1</sup>); λ<sub>max</sub> (CH<sub>3</sub>OH) 591 nm (ε = 1.55 × 10<sup>5</sup> M<sup>-1</sup> cm<sup>-1</sup>); HRMS (ESI) *m/z* 553.2125 (calcd for C<sub>34</sub>H<sub>37</sub>N<sub>2</sub>Se<sup>+</sup>: 553.2116). Anal. Calcd for C<sub>34</sub>H<sub>37</sub>N<sub>2</sub>Se·PF<sub>6</sub>: C, 58.54; H, 5.35; N, 4.02. Found: C, 58.28; H, 5.54; N, 4.03.

**Preparation of 3,6-Bis(dimethylamino)-9-(2,4,6-trimethylphenyl)-9H-xanthen-9-ylum Hexafluorophosphate (10-O).** 2-Bromomesitylene (1.35 mL, 8.85 mmol) was added to a stirred suspension of magnesium turnings (0.13 g, 5.5 mmol) in dry THF (3 mL) under a dry N<sub>2</sub> atmosphere. The mixture was stirred at ambient temperature for 1 h, and the resulting solution of Grignard reagent was transferred via cannula to a stirred suspension of 3,6-bis(dimethylamino)-9H-xanthen-9-one<sup>29</sup> (11-O, 0.100 g, 0.354 mmol) in dry THF (7 mL). The resulting solution was heated at reflux for 16 h, cooled to ambient temperature, and then poured into 25 mL of 10% (by weight) aqueous HPF<sub>6</sub>. After 12 h, the resulting precipitate was collected via filtration and washed with water (5 mL) and diethyl ether (15 mL). The residue was purified by chromatography on SiO<sub>2</sub> eluted with 20% EtOAc/hexanes to remove starting xanthone and then 10% ether/CH<sub>2</sub>Cl<sub>2</sub> to collect the product. The product was recrystallized from 9:1 CH<sub>3</sub>CN/diethyl ether to give 0.032 g (18%) of the desired product as a green solid, mp 254–255 °C: <sup>1</sup>H NMR (500 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.17 (d, 2 H, J = 9.0 Hz), 7.10 (s, 2 H), 6.90 (dd, 2 H, J = 2.5, 9.5 Hz), 6.84 (d, 2 H, J = 2.0 Hz), 3.30 (s, 12 H), 2.42 (s, 3 H), 1.90 (s, 6 H); <sup>13</sup>C{<sup>1</sup>H} NMR (125.7 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 160.2, 158.3, 158.0, 140.2, 135.9, 131.3, 129.1, 128.6, 114.9, 114.0, 96.9, 41.2, 21.3, 19.8; λ<sub>max</sub> (MeOH) 537 nm (ε = 1.18 × 10<sup>5</sup> M<sup>-1</sup> cm<sup>-1</sup>); λ<sub>max</sub> (CH<sub>2</sub>Cl<sub>2</sub>) 537 nm (ε = 1.24 × 10<sup>5</sup> M<sup>-1</sup> cm<sup>-1</sup>); HRMS (ESI) *m/z* 385.2265 (calcd for C<sub>26</sub>H<sub>29</sub>N<sub>2</sub>O<sup>+</sup>: 385.2274). Anal. Calcd for C<sub>26</sub>H<sub>29</sub>N<sub>2</sub>O·PF<sub>6</sub>: C, 58.87; H, 5.51; N, 5.28. Found: C, 58.94; H, 5.61; N, 5.28.

**Preparation of 3,6-Bis(dimethylamino)-9-(2,4,6-trimethylphenyl)-9H-thioxanthen-9-ylum Hexafluorophosphate (10-S).** 2-Bromomesitylene (0.77 mL, 5.0 mmol) was dissolved in dry THF (3 mL) under a dry N<sub>2</sub> atmosphere. Magnesium turnings (130 mg, 5.5 mmol) were added, and the resulting mixture was stirred at ambient temperature for 1 h. The resulting solution of Grignard reagent was transferred via cannula to a stirred solution of 3,6-bis(dimethylamino)-9H-thioxanthene-9-one<sup>30</sup> (11-S, 100 mg, 0.335 mmol) in dry THF (7 mL). The resulting solution was heated at reflux for 16 h, cooled to ambient temperature, and then poured into 25 mL of 10% (by weight) aqueous HPF<sub>6</sub>. After 12 h, the resulting precipitate was collected via filtration and washed with water (5 mL) and diethyl ether (15 mL). The CH<sub>3</sub>CN-soluble material was filtered through Celite, concentrated, and recrystallized from 9:1 CH<sub>3</sub>CN/diethyl ether to give 0.112 g (61%) of 10-S as a green solid, mp >260

°C: <sup>1</sup>H NMR (500 MHz, CH<sub>2</sub>Cl<sub>2</sub>) δ 7.34 (d, 2 H, J = 10.0 Hz), 7.11 (d, 2 H, J = 2.0 Hz), 7.10 (s, 2 H), 6.92 (dd, 2 H, J = 2.0, 10.0 Hz), 3.24 (s, 12 H), 2.43 (s, 3H), 1.84 (s, 6 H); <sup>13</sup>C{<sup>1</sup>H} NMR (125.7 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 161.6, 154.2, 144.8, 139.8, 136.0, 135.6, 132.0, 129.1, 119.1, 116.2, 105.9, 40.9, 21.3, 19.7; λ<sub>max</sub> (MeOH) 558 nm (ε = 1.03 × 10<sup>5</sup> M<sup>-1</sup> cm<sup>-1</sup>); λ<sub>max</sub> (CH<sub>2</sub>Cl<sub>2</sub>) 557 nm (ε = 1.24 × 10<sup>5</sup> M<sup>-1</sup> cm<sup>-1</sup>); HRMS (ESI) *m/z* 401.2044 (calcd for C<sub>26</sub>H<sub>29</sub>N<sub>2</sub>S<sup>+</sup>: 401.2046); Anal. Calcd for C<sub>26</sub>H<sub>29</sub>N<sub>2</sub>S·PF<sub>6</sub>: C, 57.14; H, 5.35; N, 5.13. Found: C, 57.41; H, 5.15; N, 5.12.

**Photocatalyzed Aza-Henry Reaction of 2-Phenyl-1,2,3,4-tetrahydroisoquinoline (5a).** *Comparison of Photocatalysts.* To a 4-dram (15 mL) vial were added 0.063 g (0.30 mmol) of tetrahydroisoquinoline 5a (0.063 g, 0.30 mmol) and 0.003 mmol (1 mol %) of photocatalyst. The contents were dissolved in 5 mL of a 4:1 mixture of MeCN/MeNO<sub>2</sub>. The reaction mixture was then irradiated with stirring for 3.0 h with a GE 14 W, 850 lm LED light placed 1 cm from the 4-dram vial. The reaction mixture was concentrated in vacuo, and the % conversion was determined via <sup>1</sup>H NMR spectroscopy comparing the integral of the 2-nitromethyl methylene protons (δ 4.81 and 4.53) and the 2-methine proton (δ 5.51) of 6a with the 2-methylene protons (δ 4.42) of 5a. The reactions were run in triplicate, and values reported in Table 1 represent the mean of the three runs ± the standard deviation (SD) for the three runs.

**Preparative Conversion of 2-Phenyl-1,2,3,4-tetrahydroisoquinoline (5a) to 1-Nitromethyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline (6a).** *A. 7-Se as Photocatalyst.* To a 4-dram vial were added tetrahydroisoquinoline 5a (0.210 g, 1.00 mmol) and 7-Se (5.5 mg, 0.010 mmol, 1 mol %). The contents were dissolved in 15 mL of a 4:1 mixture of MeCN/MeNO<sub>2</sub>. The reaction mixture was then irradiated with stirring for 11.0 h with a GE 14 W, 850 lm LED light placed 1 cm from the 4-dram vial. At the completion of irradiation, the reaction mixture was concentrated in vacuo and the residue was partitioned between a mixture of ether (20 mL) and water (20 mL). The organic phase was separated, and the aqueous layer was further extracted with ether (2 × 10 mL). The combined organic extracts were dried over anhydrous MgSO<sub>4</sub> and concentrated in vacuo. The crude product was purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.212 g (84%) of 6a<sup>5</sup> and 0.037 g (16%) of dihydroisoquinolone 13a.<sup>32</sup>

*B. 10-Te as Photocatalyst.* The reaction was repeated using photocatalyst 10-Te (6.0 mg, 0.010 mmol, 1 mol %) with 5 h of irradiation. Products 6a<sup>5</sup> and 13a<sup>32</sup> were purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.22 g (85%) of 6a<sup>5</sup> and 0.005 g (2%) of dihydroisoquinolone 13a.<sup>32</sup>

**For 6a:**<sup>5</sup> colorless oil; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.08–7.28 (m, 4 H), 6.95 (d, 2 H, J = 7.5 Hz), 6.82 (t, 2 H, J = 7 Hz), 5.52 (t, 1 H, J = 7 Hz), 4.82 (dd, 1 H, J = 7.5, 11.7 Hz), 4.54 (dd, 1 H, J = 6.5, 11.7 Hz), 3.60 (m, 2 H), 3.04 (m, 1 H), 2.75 (m, 1 H); <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz, CDCl<sub>3</sub>) δ 148.3, 135.2, 132.8, 129.5, 129.4, 129.3, 128.0, 126.9, 119.3, 115.0, 78.6, 58.1, 41.9, 26.3.

**For 13a:**<sup>32</sup> white solid, mp 119–120 °C (lit.<sup>33</sup> mp 119–123 °C); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.20 (d, 1 H, J = 7.5 Hz), 7.55–7.35 (m, 7 H), 7.27 (m, 1 H), 4.02 (t, 1 H, J = 6.5 Hz), 3.17 (t, 1 H, J = 6.5 Hz); <sup>13</sup>C{<sup>1</sup>H} NMR (125.7 MHz, CDCl<sub>3</sub>) δ 164.5, 143.5, 132.4, 130.1, 129.2, 129.0, 127.5, 127.3, 126.5, 125.6, 49.7, 28.9; MS (ESI) *m/z* 224 (calcd for C<sub>15</sub>H<sub>13</sub>NO<sup>+</sup>: 224).

**Preparative Conversion of 2-(4-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline 5b to 1-Nitromethyl-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (6b).**<sup>5</sup> *A. 7-Se as Photocatalyst.* To a 4-dram vial were added tetrahydroisoquinoline 5b (0.240 g, 1.00 mmol) and 7-Se (5.5 mg, 0.010 mmol, 1 mol %). The contents were dissolved in 15 mL of a 4:1 mixture of MeCN/MeNO<sub>2</sub>. The reaction mixture was then irradiated with stirring for 8.5 h with a GE 14 W, 850 lm LED light placed 1 cm from the 4-dram vial. At the completion of irradiation, the reaction mixture was concentrated in vacuo and treated as described above for the reaction with 5a. The crude product was purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.241 g (81%) of 6b<sup>5</sup> and 0.005 g (2%) of dihydroisoquinolone 13b.<sup>2</sup>



**B. 10-Te as Photocatalyst.** The reaction was repeated using photocatalyst **10-Te** (6.0 mg, 0.010 mmol, 1 mol %) with 6.5 h of irradiation. Products **6a**<sup>5</sup> and **13a**<sup>32</sup> were purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.224 g (75%) of **6b**<sup>5</sup> and 0.003 g (1%) of dihydroisoquinoline **13b**.<sup>32</sup>

**For 6b:**<sup>5</sup> colorless oil; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.08–7.28 (m, 4 H), 6.90 (d, 2 H, *J* = 9 Hz), 6.80 (d, 2 H, *J* = 9 Hz), 5.38 (dd, 1 H, *J* = 6, 8.5 Hz), 4.80 (dd, 1 H, *J* = 8.5, 11.7 Hz), 4.54 (dd, 1 H, *J* = 6, 11.7 Hz), 3.73 (s, 3 H), 3.55 (m, 2 H), 3.00 (m, 1 H), 2.67 (m, 1 H); <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz, CDCl<sub>3</sub>) δ 153.8, 142.9, 135.3, 132.7, 129.3, 127.7, 126.8, 126.4, 118.6, 114.5, 78.7, 58.7, 55.4, 42.8, 25.6.

**For 13b:**<sup>32</sup> white solid, mp 116–119 °C (lit.<sup>32</sup> mp 120–121 °C); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.14 (d, 1 H, *J* = 7.5 Hz), 7.45 (td, 1 H, *J* = 1.6, 7.5 Hz), 7.37 (t, 1 H, *J* = 7.5 Hz), 7.20–7.32 (m, 4 H), 3.94 (t, 1 H, *J* = 6.5 Hz), 3.82 (s, 3 H), 3.13 (t, 1 H, *J* = 6.5 Hz); <sup>13</sup>C{<sup>1</sup>H} NMR (125.7 MHz, CDCl<sub>3</sub>) δ 164.4, 157.8, 138.3, 136.1, 131.9, 129.8, 128.7, 127.1, 126.9, 126.7, 114.2, 55.5, 49.7, 28.7; MS (ESI) *m/z* 254 (calcd for C<sub>16</sub>H<sub>15</sub>NO<sub>3</sub>+H<sup>+</sup>: 254).

**Preparative Conversion of 2-(4-Chlorophenyl)-1,2,3,4-tetrahydroisoquinoline (5c) to 1-Nitromethyl-2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinoline (6c).** **A. 7-Se as Photocatalyst.** To a 4-dram vial were added tetrahydroisoquinoline **5c** (0.245 g, 1.00 mmol) and **7-Se** (5.5 mg, 0.010 mmol, 1 mol %). The contents were dissolved in 15 mL of a 4:1 mixture of MeCN/MeNO<sub>2</sub>. The reaction mixture was then irradiated with stirring for 5.0 h with a GE 14 W, 850 lm LED light placed 1 cm from the 4-dram vial. At the completion of irradiation, the reaction mixture was concentrated in vacuo and treated as described above for **5**. The crude product was purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.187 g (62%) of **6c**<sup>5</sup> and 0.043 g (17%) of dihydroisoquinoline **13c**.<sup>32</sup>

**B. 10-Te as Photocatalyst.** The reaction was repeated using photocatalyst **10-Te** (6.0 mg, 0.010 mmol, 1 mol %) with 6.5 h of irradiation. The products **6c**<sup>5</sup> and **13c**<sup>32</sup> were purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.25 g (85%) of **6c**<sup>5</sup> and 0.005 g (2%) of dihydroisoquinoline **13c**.<sup>32</sup>

**For 6c:**<sup>5</sup> colorless oil; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.26–7.34 (m, 4 H), 6.89 (dd, *J* = 1.5, 6.3 Hz), 5.48 (m, 1 H), 4.84 (ddd, 1 H, *J* = 1.2, 8.4, 12.1 Hz), 4.56 (ddd, 1 H, *J* = 1.5, 5.4, 12.1 Hz), 3.62 (m, 2 H), 3.06 (m, 1 H), 2.78 (m, 1 H).

**For 13c:**<sup>32</sup> white solid, mp 150–152 °C (lit.<sup>33</sup> mp 150–151.5 °C); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.14 (d, 1 H, *J* = 7.6 Hz), 7.48 (dt, 1 H, *J* = 1.2, 7.6 Hz), 7.40–7.32 (m, 5 H), 7.24 (d, 1 H, *J* = 9.6 Hz), 3.97 (t, 2 H, *J* = 6.4 Hz), 3.14 (t, 2 H, *J* = 6.4 Hz); <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz, CDCl<sub>3</sub>) δ 164.2, 141.5, 138.2, 132.2, 131.5, 129.4, 128.9, 128.7, 127.2, 126.9, 126.5, 49.2, 28.5.

**Preparation of 2-(Nitromethyl)-1-phenylpyrrolidine 6d.**<sup>5</sup> **A. 7-Se as Photocatalyst.** To a 4-dram vial equipped with a stir bar were added 1-phenylpyrrolidine **5d** (0.086 mL, 0.60 mmol) and 1 mol % of photocatalyst **7-Se** (5.5 mg, 0.010 mmol, 1 mol %). The contents were dissolved in 5 mL of a 4:1 mixture of MeCN/MeNO<sub>2</sub>. The reaction mixture was irradiated for 90 h with a GE 14 W, 850 lm LED light. The reaction mixture was then concentrated in vacuo. Product **6d** was purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.0038 g (3.1% yield) of **6d**.

**B. 10-Te as Photocatalyst.** The reaction was repeated using photocatalyst **10-Te** (6.0 mg, 0.010 mmol, 1 mol %). The product **6d** was purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.0075 g (6% yield) of **6d**.

**For 6d:**<sup>5</sup> <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.34–7.24 (m, 2H), 6.79 (t, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 2H), 4.68–4.59 (m, 1H), 4.48–4.38 (m, 1H), 4.19 (t, *J* = 10.5 Hz, 1H), 3.51–3.44 (m, 1H), 3.27–3.14 (m, 1H), 2.18–2.04 (m, 1H); <sup>13</sup>C{<sup>1</sup>H} NMR (300 MHz, CDCl<sub>3</sub>): 145.5, 129.7, 117.3, 111.9, 75.8, 57.4, 48.1, 29.3, 22.8.

**Preparation of 3,4-Dihydro-2-phenyl-1(2H)-isoquinolinone 13a.**<sup>32</sup> **A. 7-Se as Photocatalyst.** In a 4-dram vial equipped with a stir bar, 2-phenyl-1,2,3,4-tetrahydroisoquinoline **5a** (0.209 g, 1.00 mmol) and **7-Se** (5.5 mg, 0.010 mmol, 1 mol %) were dissolved in 15 mL of a 4.9:0.1 mixture of MeCN/H<sub>2</sub>O. The reaction mixture was irradiated with a GE 14 W, 850 lm LED light for 8 h. The crude

product was purified via chromatography on SiO<sub>2</sub> eluted with 20% EtOAc/hexanes. Isoquinolinone **13a** was recrystallized from dichloromethane/diethyl ether to yield 0.129 g (58% isolated yield) of **13a**.

**B. 10-Te as Photocatalyst.** The reaction was repeated using photocatalyst **10-Te** (6.0 mg, 0.010 mmol, 1 mol %) with irradiation for 8 h. Isoquinolinone **13a** was purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.141 g (63% isolated yield) of **13a**.

**C. 7-S as Photocatalyst.** The reaction was repeated using photocatalyst **7-S** (5.2 mg, 0.010 mmol, 1 mol %) with irradiation for 12 h. Unreacted **5a** (0.19 g, 90%) was recovered from the reaction mixture.

**D. 10-S as Photocatalyst.** The reaction was repeated using photocatalyst **10-S** (5.3 mg, 0.010 mmol, 1 mol %) with irradiation for 12 h. Unreacted **5a** (0.20 g, 95%) was recovered from the reaction mixture.

**Preparation of 3,4-Dihydro-2-(4-methoxyphenyl)-1(2H)-isoquinolinone 13b.**<sup>32</sup> **A. 7-Se as Photocatalyst.** In a 4-dram vial equipped with a stir bar, **5b** (0.239 g, 1.00 mmol) and **7-Se** (5.5 mg, 0.010 mmol, 1 mol %) were dissolved in 15 mL of a 4.9:0.1 mixture of MeCN/H<sub>2</sub>O. The reaction mixture was irradiated with a GE 14 W, 850 lm LED light for 13 h. The crude product was purified via chromatography on SiO<sub>2</sub> eluted with 20% EtOAc/hexanes. Isoquinolinone **13b** was recrystallized from dichloromethane/diethyl ether to yield 0.098 g (41% isolated yield) of **13b**.

**B. 10-Te as Photocatalyst.** The reaction was repeated using photocatalyst **10-Te** (6.0 mg, 0.010 mmol, 1 mol %) with irradiation for 8 h. Isoquinolinone **13b** was purified via chromatography on SiO<sub>2</sub> eluted with 5% EtOAc in hexanes to yield 0.18 g (75% isolated yield) of **13b**.

**Preparation of 3,4-Dihydro-2-(4-chlorophenyl)-1(2H)-isoquinolinone 13c.**<sup>32</sup> **Using 7-Se as Photocatalyst.** In a 4-dram vial equipped with a stir bar, **5b** (0.244 g, 1.00 mmol) and **7-Se** (5.5 mg, 0.010 mmol, 1 mol %) were dissolved in 15 mL of a 4.9:0.1 mixture of MeCN/H<sub>2</sub>O. The reaction mixture was irradiated with a GE 14 W, 850 lm LED light for 7.5 h. The white precipitate was collected by filtration, and the filtrate was then concentrated in vacuo. The crude product was purified via chromatography on SiO<sub>2</sub> eluted with 20% EtOAc/hexanes. Isoquinolinone **13c** was recrystallized from dichloromethane/diethyl ether to yield 0.121 g (78% isolated yield) of **13c**. The white precipitate was isolated in 0.031 g (6%) yield and was identified as a mixture of *D,L*- and *meso*-diastereomers of the peroxodimer **14a**: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.32–7.06 (m, 12 H), 6.82 (t, 4 H, *J* = 7.4 Hz), 6.09 (s, 1 H, one diastereomer), 5.98 (s, 1H, one diastereomer), 3.59–3.46 (m, 1H), 3.42–3.18 (m, 3H), 2.88–2.69 (m, 4H); <sup>13</sup>C{<sup>1</sup>H} NMR (300 MHz, CDCl<sub>3</sub>) δ 146.8, 146.7, 136.0, 131.91, 131.88, 128.5, 128.4, 128.36, 128.33, 128.2, 127.4, 127.3, 125.7, 123.6, 123.5, 115.7, 90.2, 90.0, 42.2, 27.50, 27.46; MS (ESI) *m/z* 242 (calcd for C<sub>15</sub>H<sub>13</sub><sup>35</sup>ClN<sup>+</sup>: 242; calcd for C<sub>30</sub>H<sub>26</sub><sup>35</sup>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>+H<sup>+</sup>: 517). Anal. Calcd for C<sub>30</sub>H<sub>26</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>: C, 69.64; H, 5.06; N, 5.41. Found: C, 69.98; H, 4.92; N, 5.41. Organic peroxide species are potentially explosive and care should be taken handling these compounds.

**Photo-oxidation of 5a with Photocatalyst 10-S in 4.9:0.1 CH<sub>3</sub>CN/8.8 M H<sub>2</sub>O<sub>2</sub>.** In a 4-dram vial equipped with a stir bar, 2-phenyl-1,2,3,4-tetrahydroisoquinoline **5a** (0.209 g, 1.00 mmol) and **10-S** (5.3 mg, 0.010 mmol, 1 mol %) were dissolved in 15 mL of a 4.9:0.1 mixture of MeCN/8.8 M H<sub>2</sub>O<sub>2</sub> (final concentration of H<sub>2</sub>O<sub>2</sub> of 0.18 M). The reaction mixture was irradiated with a GE 14 W, 850 lm LED light for 8 h and the reaction mixture was concentrated in vacuo.

**Quantum Yields for Fluorescence and Singlet Oxygen Generation.** Optical absorption measurements were performed using PerkinElmer Lambda 900 UV–vis-NIR spectrophotometer. A Fluorolog-3 spectrofluorimeter equipped with iHR320 spectrometer for infrared range (Horiba) was employed to obtain fluorescence spectra. Absorption for all the measured samples was matched at the wavelength of excitation (532 nm) before spectra acquisition.

To quantify singlet oxygen generation, singlet oxygen phosphorescence emission was detected by the thermoelectrically cooled NIR-

PMT unit (Hamamatsu H10330B-75) attached to the output of the iHR320 spectrometer that was set to 1270 nm. Singlet oxygen decay under pulsed excitation was directly recorded on the Tektronix oscilloscope (TDS 3034C Digital Phosphor oscilloscope) coupled to the NIR-PMT unit. A second harmonic (532 nm) from nanosecond pulsed Q-switched Nd:YAG laser (LS-2137 from Lotis TII) lasing at the SH with repetition rate of 10 Hz was used as an excitation source.

**Data Analysis and Statistics.** Statistical significance was assessed using one-way ANOVA and a posthoc multiple pairwise comparison using the Tukey test with a significance level of 0.05. The Student's *t* test was used for pairwise comparisons of independent samples. All *t* tests were two-sided, and *p* values less than 0.05 were considered significant.

**Computational Details.** Calculations were done with Gaussian09<sup>36</sup> input files, and results were visualized using GaussView05.<sup>48</sup> All structures were optimized using the B3LYP<sup>37–39</sup> level of theory with the 6-31+G(d)<sup>40–42</sup> basis set for all light atoms and LanL2DZ<sup>43–45</sup> for Te. Energy values were obtained from the free energy from the frequency calculations.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organo-  
met.9b00126.

Text and figures giving general methods, experimental data for the synthesis of **5a**, **5b**, and **5c**, NMR spectral data (<sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} NMR) for all noncommercial compounds, and <sup>1</sup>H NMR spectral data for the mixture of products from irradiation of **5a** and **10-Te** in 4.9:0.1 CH<sub>3</sub>CN/H<sub>2</sub>O and from **5** and **10-S** in 4.9:1 CH<sub>3</sub>CN/8.8 M H<sub>2</sub>O<sub>2</sub> (PDF)

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### Notes

The authors declare no competing financial interest.

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