Supporting Information

Structure-Reactivity Studies, Characterization, and Transformation of Intermediates by Lithium Chloride in the Direct Insertion of Alkyl and Aryl Iodides to Metallic Zinc Powder

Chao Feng, Quinn T. Easter, Suzanne A. Blum[*]

Department of Chemistry, University of California, Irvine, California, 92697-2025, United States

I. General Considerations

All manipulations were carried out under a nitrogen atmosphere using dried glassware unless otherwise noted. All chemicals were used as received from commercial sources unless otherwise noted. THF, toluene, and dichloromethane were HPLC grade and were purchased from Fisher Chemical, and were dried by passage through an alumina column under argon pressure on a Seca Solvent System (Glass Contour). DMF was obtained from EMD Millipore and used as received. Zinc powder (99.9%) was purchased from Strem (325 mesh, 99.9%) and dried in vacuo while applying heat from a heat gun for ca. 30 min.[1,2] Lithium chloride was purchased from Sigma-Aldrich and dried while applying heat from a flame before use. Tetra-*n*-butylammonium chloride was purified by recrystallization from acetone/ether and dried in vacuo. 3,4-Dichlorobenzaldehyde was purified by recrystallization from ethanol. 4-Iodophenylacetic acid was purchased from Alfa Aesar and used as received. Zinc(II) iodide (>98%) was purchased from Sigma Aldrich and used directly from the bottle. Zinc(II) chloride was purchased from Fischer and purified by refluxing in dioxane over zinc dust, the solution was then filtered hot to result in precipitation the zinc(II) chloride, which was then recrystallized from dioxane. Flash chromatography was conducted using a Teledyne Isco Combiflash Rf 200 Automated Flash Chromatography System.

II. Fluorescence Microscopy

Microscopy and Image Acquisition. Imaging was performed with an IX71 inverted microscope (Olympus Corporation) and an oil-immersion objective with a 1.49 numerical aperture. Samples were illuminated with the 488 nm line of an Ar/Kr ion laser (Coherent Inc.) set to 25 mW.

Illumination was done under conditions of EPI. Samples were imaged with a C9100-13 electron multiplier CCD camera (Hamamatsu Photonics). The CCD chip was a back-thinned electron multiplication type with an effective 512×512 array of pixels.

Coverslip Preparation. Glass coverslips (25×25 mm, No. 1.5, VWR Scientific) with a thickness of 0.17 mm were used for imaging. Cleaning of the coverslips was done by soaking them in a polypropylene Coplin staining jar (VWR Scientific) with a 0.5% (v:v) solution of Hellmanex Detergent (Fisher Scientific) in MilliQ water for 24 h, then sonicating them in the same solution for 30 min. The coverslips were then rinsed three times, first with MilliQ water, then spectroscopic grade ethanol; finally they were dried with a heat gun.

Construction of Reaction Cells. Reaction cells were constructed from a 1 dram vial by cutting of the bottom of the vials and adhering it to the prepared glass coverslip with Devcon 5 Minute® Epoxy (Figure S1). After allowing the epoxy to cure for 1 h, the reaction cells were then dried under dynamic vacuum for 12 h before being brought into the glovebox.

Figure S1. A picture of a typical reaction cell used.

Construction of Salt Pocket. The salt pocket allowed for the addition of solids to the imaging cell without compromising the atmosphere. The pocket was made by heating the tapered section of a Pasteur pipette with a blowtorch. Once the glass was molten (and had the consistency of cooked spaghetti) the delivering end of the pipette was then slowly pulled away from the base of

the pipette while gently twisted (Figure S2). To fit inside the reaction cell, the open end of the pipette was scored and removed by holding firmly and applying pressure with your thumbs. NOTE: It is important that the pocket is as long as possible, yet still able to fit inside the 1 dram imaging cell. Otherwise it has been noticed to lead to contamination of the sample as a result of the surface adhesion of THF, which allows for THF to travel up the side of the glass and into the pocket.
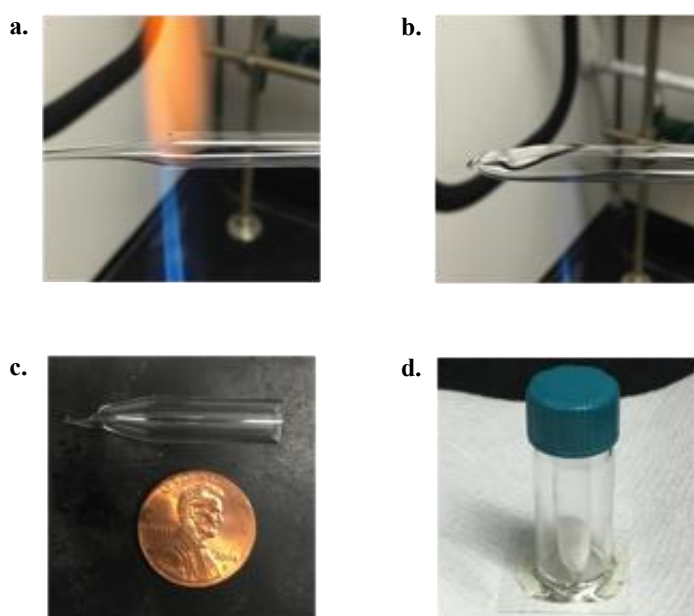

Figure S2. Images depicting construction of the salt pocket. (a) Shows the location of where to heat the pipette, (b) what the pocket should look like after sealing, (c) the finished salt pocket after scoring and removal of excess glass, (d) a typical reaction cell with a salt pocket inside.

II. Triplicate Data LiCl Addition to Aryl Iodide Derived Surface Intermediates

The cells were imaged for 11 min each. Zinc particles with fluorescent signals were found and kept in focus. After imaging the reaction cell for 40 s and observing the surface bound

intermediate, the lithium chloride was added by inverting the cell and gently shaking the cell, this was repeated three times. After putting the cell back onto the microscope, zinc particles were found and brought into focus at 100 s after the salt addition and these particles were kept in focus until 540 s after the addition, after which the stage was moved to find new zinc particles that had not yet been exposed to laser illumination for the 600 s image.

Figure S3a-c shows the results from triplicate lithium chloride addition experiments. All triplicate runs show the same trends. Data from the triplicate runs in Figure S3 are displayed at identical contrast settings in order to show the variation in brightness that originates from the measurement on heterogeneous samples (2500-25000 brightness units). Although the absolute brightness is somewhat variable between experiments on account of the heterogeneity of the samples, the *trend* of lithium chloride reactivity is identical. All samples start with significant fluorescent material on the surface, as seen as bright green spots of fluorescent on the dark zinc particles. Addition of lithium chloride induces the complete removal of this material after 600 s, observed as the complete lack of bright green fluorescent spots on the surface of the dark zinc particles after this time.
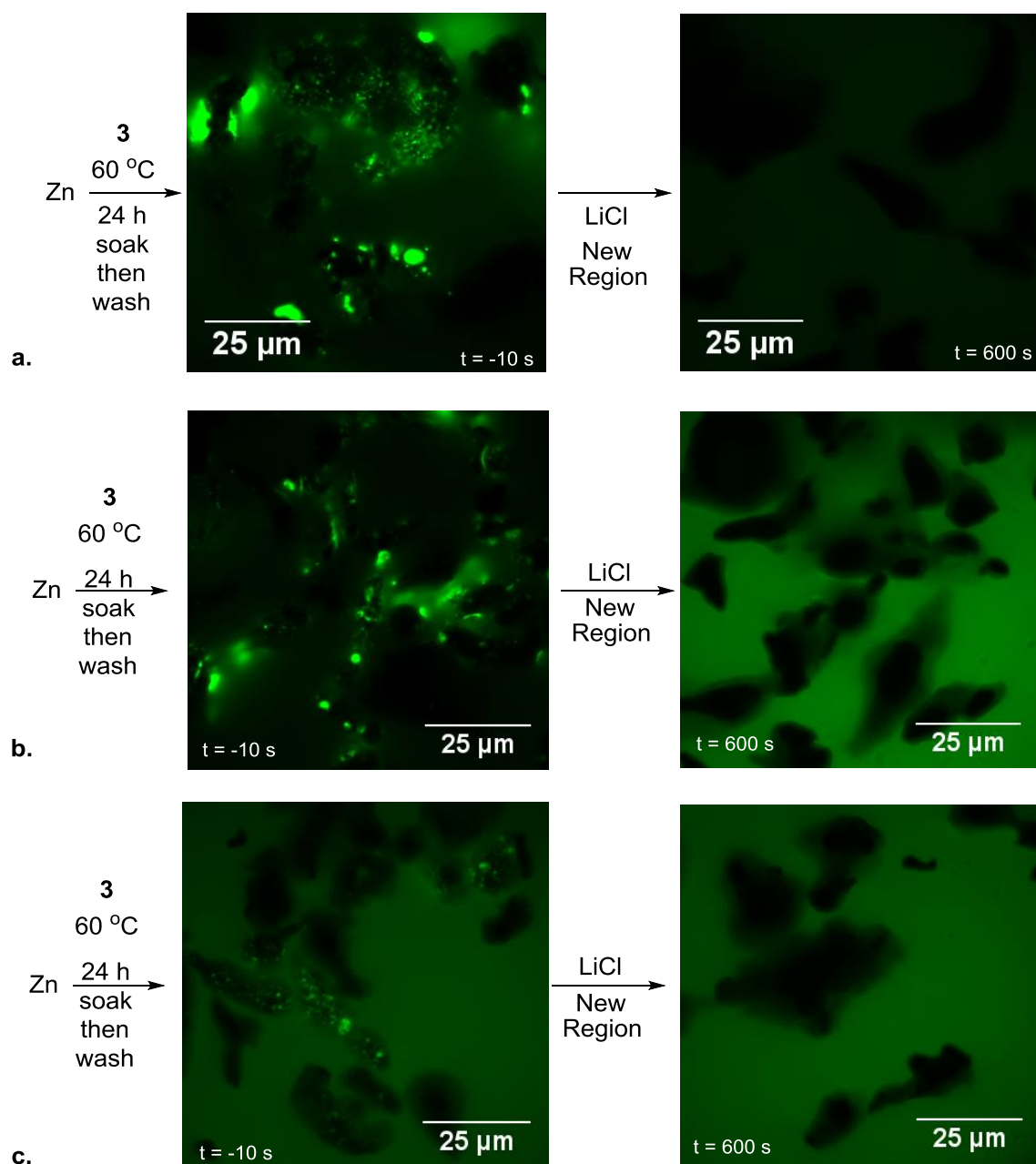
Figure S3a-c. Results from triplicate lithium chloride addition experiments; *a* is the same data set shown in Figure 4b in the manuscript. All images are displayed at identical contrast settings in order to show the variation in brightness between samples originating from the heterogeneous samples. All triplicate runs show the same trends.

III. Quantum Yield and Spectra of Organozinc-BODIPY Compound

*Quantum yield of organozinc compound **6** in THF.* To 5,5-difluoro-10-(4-iodobutyl)-1,3,7,9-tetramethyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-4-ium-5-uide (**1**) (13.8 mg, 0.0321 mmol) in dry THF (2 mL) was added LiCl (1.4 mg, 0.032 mmol) and zinc powder (4.2 mg, 0.064 mmol) and stir bar inside the glovebox. The resulting reaction mixture was stirred at room temperature for 1 h inside the glovebox, at which time 0.2 mL of the clear solution was taken for GC-MS analysis to confirm full conversion of **1** into organozinc species **6**. Then the clear solution above the reaction mixture was removed by pipet and diluted in dry THF in a vial inside the glovebox, which was used as the stock solution for measuring the quantum yield of organozinc species **6** in a sealable cuvette. For each measurement, different numbers of drops of the stock solution were taken by pipet and diluted in dry THF in a sealable cuvette inside the glovebox. The cuvette was sealed with a cap and removed from the glovebox for measurement. Rhodamine 6G in EtOH (Φ = 0.95)[3] and Fluorescein in 0.1 M NaOH (aq) (Φ = 0.925)[1] were used as standards (Figure S4). The quantum yield of organozinc compound **6** in THF is Φ = 0.52. Absorption and emission spectra of organozinc compound **6** are shown in Figure S5.
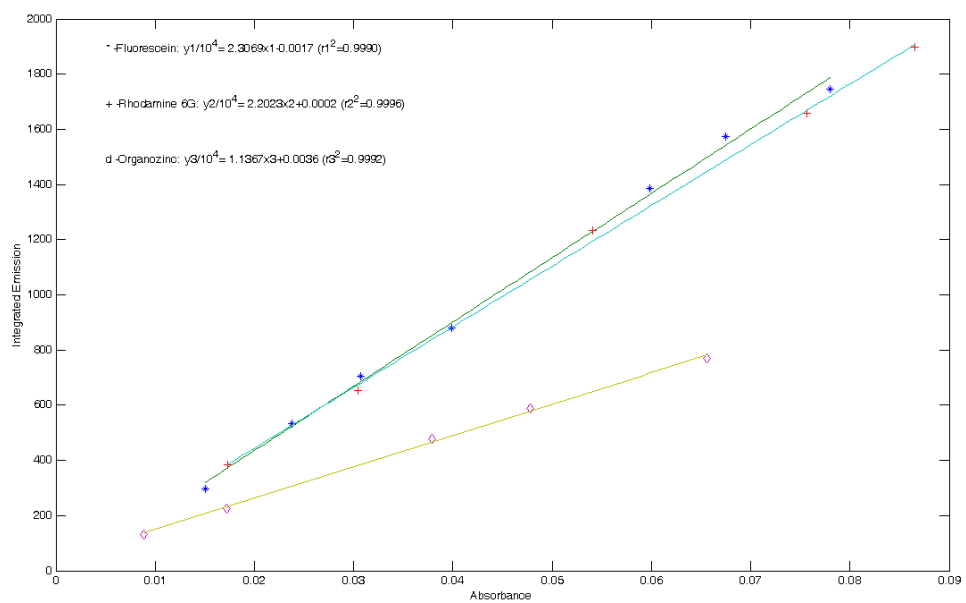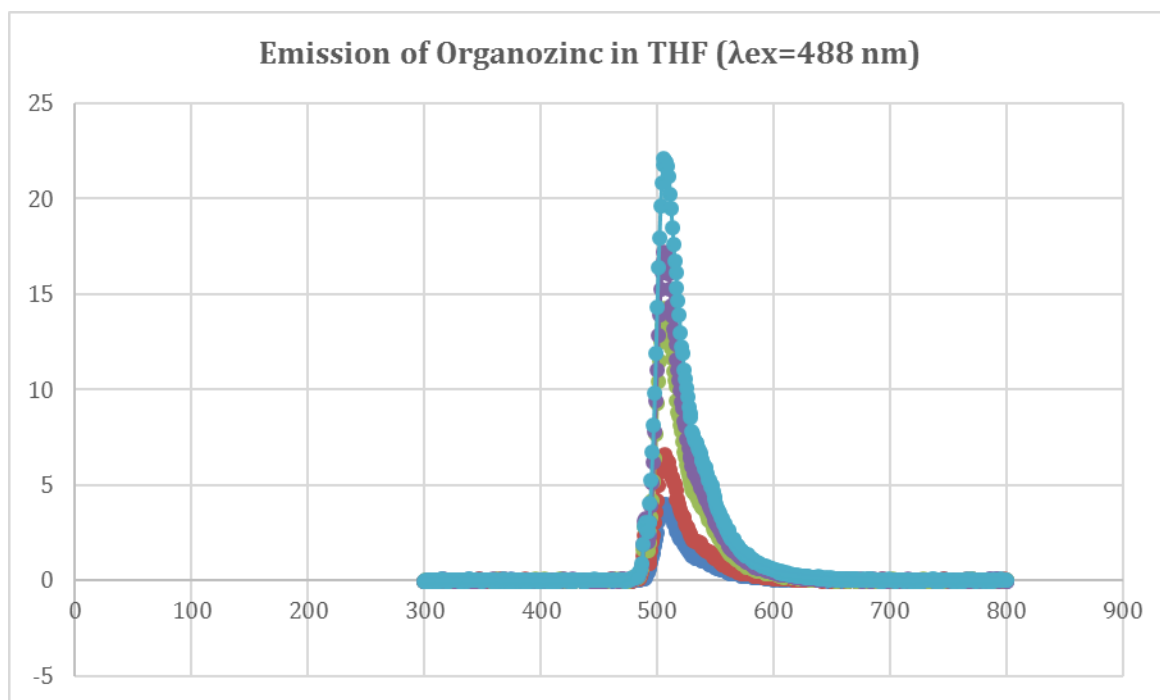
Figure S4. Measurement of quantum yield of organozinc compound **6** in THF with comparison with standards.
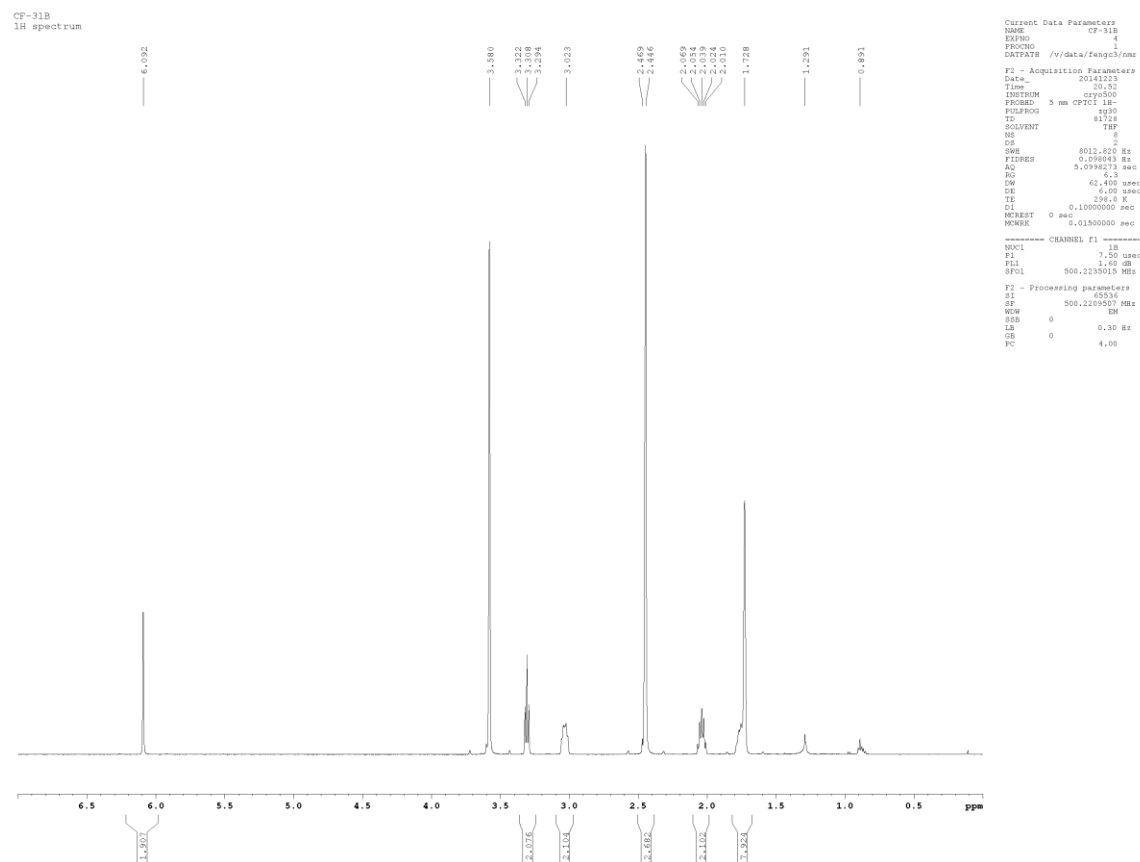

a.
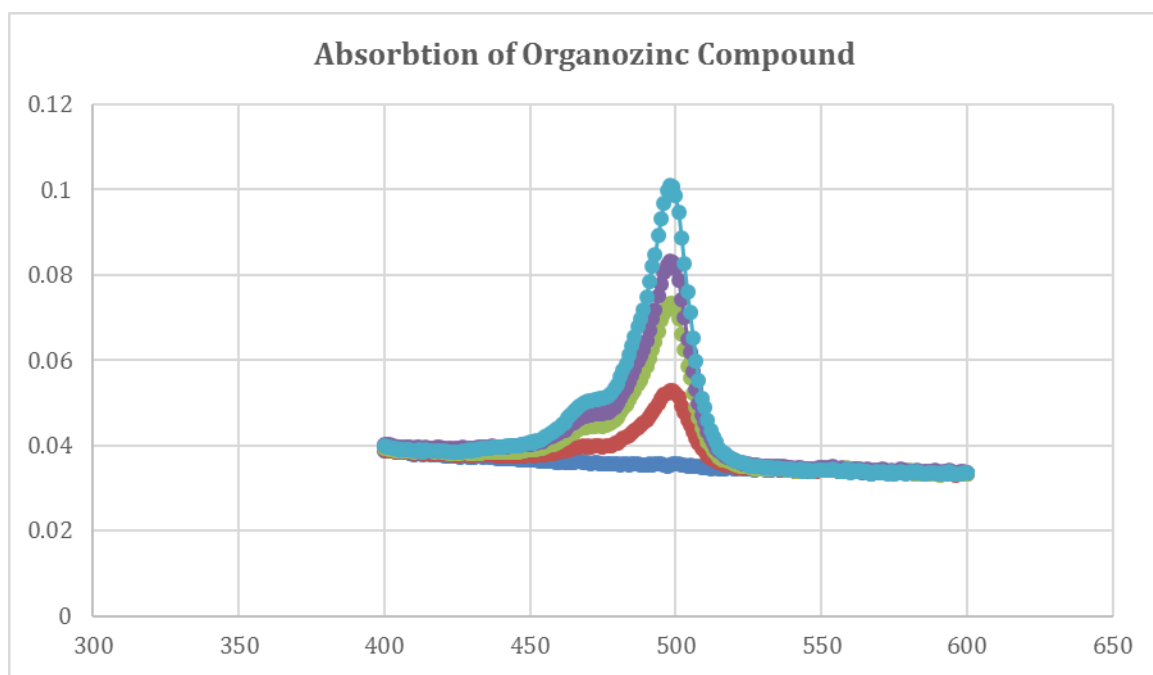
λm = 498 nm

λm = 506 nm

**Figure S5**. Absorbance (a. u.) vs. nm. a) Absorption and b) emission spectra of organozinc compound **6**.

A separate sample of organozinc compound for ^{1}H NMR spectroscopic analysis was prepared in situ in THF-d_8. To 5,5-difluoro-10-(4-iodobutyl)-1,3,7,9-tetramethyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-4-ium-5-uide (**2**) (15.6 mg, 0.0363 mmol) in dry THF-d_8 (2.0 mL) was added LiCl (2.3 mg, 0.054 mmol) and zinc powder (4.7 mg, 0.073 mmol, previously activated by TMSCl in protioTHF as described in the experimental section in the manuscript) and stir bar inside glovebox. The resulting reaction mixture was stirred at room temperature for 1 h inside glovebox and an ^{1}H NMR spectrum was taken using the 0.8 mL upper clear solution of the reaction mixture in a J-Young NMR tube. This spectrum showed full consumption of starting material **2** and formation of organozinc complex **6**. ^{1}H NMR (600 MHz, THF-d_8) δ 6.04 (br s, 2 H), 2.99 (br s, 2 H), 2.41 (br s, 6 H), 2.35 (br s, 6 H), 1.87 (br s, 2 H),

1.66 (br s, 2 H), 0.19 (br s, 2 H). This spectrum is shown in Figure S5. The other peaks are from residual protioTHF, hexane, and an unidentified species.

Figure S6. ^{1}H NMR spectrum of in situ generated **6**.

5,5-Difluoro-10-(4-iodobutyl)-1,3,7,9-tetramethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine (**2**). Compound **2** was previously reported and fully characterized in our initial communication.[1] The ^{1}H NMR spectral data are reproduced here to facilitate comparison with in situ generated **6** (described above). **2**: ^{1}H NMR (500 MHz, d_8-THF) δ 6.09 (s, 2 H), 3.31 (t, J = 7 Hz, 2 H), 3.08-3.00 (m, 2 H), 2.45 (s, 12 H), 2.04 (tt, J = 7.5, 7.5 Hz, 2 H), 1.80-1.70 (m, 2 H). Spectrum of **2** is provided in Figure S7.

Figure S7. ^{1}H NMR spectrum of previously published **2**,[1] reproduced here to facilitate direct comparison between **6** and **2**.

Quantum yield of probe 2. Absorbance and emission spectra of probe **2** were reported in our original communication.[1] Quantum yield of **2** was determined as follows: Rhodamine 6G in EtOH ($\Phi = 0.95$)[3] and fluorescein in 0.1 M NaOH (aq) ($\Phi = 0.925$) [1] were used as standards (Figure S6). The quantum yield of alkyl iodide BODIPY probe **2** in THF is $\Phi = 1.0$.
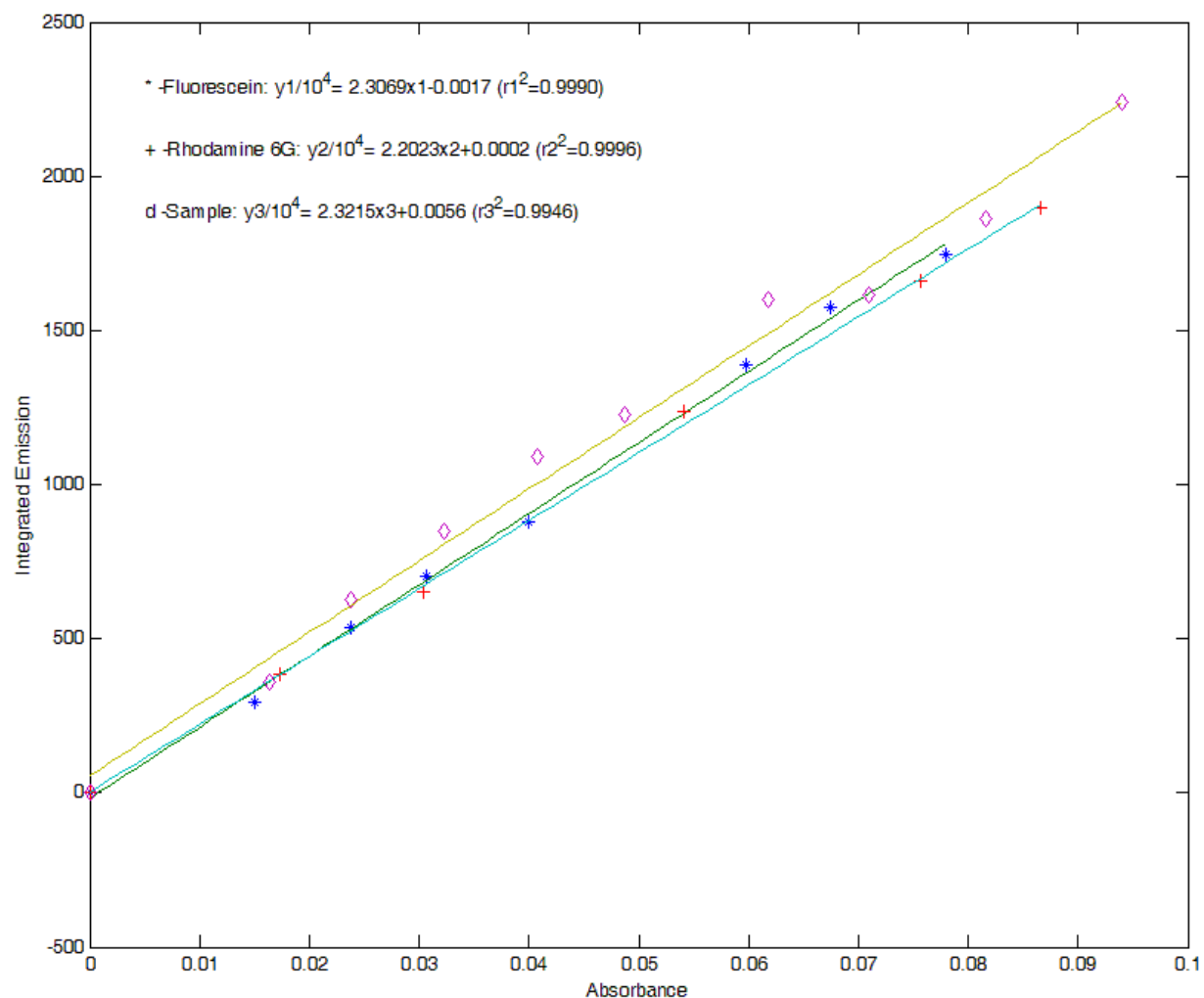
Figure S8. Measurement of quantum yield of alkyl BODIPY probe **2** in THF with comparison with standards.

IV. Tabulated EDS Data

Table 1. Zn Particles Heated but Otherwise Untreated

Point	Zn atomic %	O atomic %
1	88.83	11.17
2	92.97	7.03
3	91.81	8.19
4	100	0
5	81.19	18.71
6	86.95	13.05
7	100	0
8	85.58	14.42
9	91.83	8.17
10	97.87	2.13
11	100	0
Average	92.46	7.53
St. Dev.	6.17	6.15

Table 2. Zn Particles Treated with TMSCl for 30 min

Point	Zn atomic %	O atomic %
1	94.16	5.84
2	92.51	7.49
3	97.00	3.00
4	93.46	6.54
5	97.55	2.45
6	96.27	3.73
7	97.86	2.14
8	96.11	3.89
9	96.83	3.17
10	90.65	9.35
11	100	0
Average	95.67	4.33
St. Dev.	2.58	2.58

Table 3. Zn Particles Treated with TMSCl for 2 h

Point	Zn atomic %	O atomic %
1	100	0
2	100	0
3	91.89	8.11
4	95.54	4.46
5	89.61	10.39
6	96.78	3.22
7	97.12	2.88
8	100	0
9	100	0
10	92.02	7.98
11	100	0
Average	**96.63**	**3.37**
St. Dev.	**3.71**	**3.71**

Table 4. Zn Particles Treated with LiCl for 2 h

Point	Zn atomic %	O atomic %
1	88.65	11.35
2	88.67	11.33
3	90.94	9.06
4	100.00	0
5	89.61	10.39
6	87.23	12.77
7	89.14	10.86
8	100	0
9	88.83	11.17
10	90.65	9.35
11	100	0
Average	**92.16**	**7.84**
St. Dev.	**4.90**	**4.90**

V. References

1. Feng, C.; Cunningham, D. W.; Easter, Q. T.; Blum, S. A. *J. Am. Chem. Soc.* **2016**, *138*, 11156–11159.

2. Krasovskiy, A.; Malakohov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 6040–6044.

3. Brouwer, A. M. *Pure Appl. Chem.* **2011**, *83*, 2213–2228.