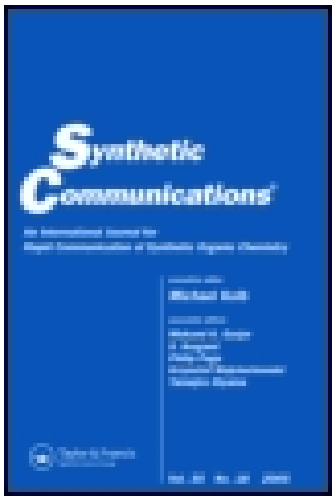

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Zeyin Zhou [a] & Weijun Yang [a]

[a] Department of Chemistry and Chemical Engineering , Hunan University , Changsha , Hunan Province , P. R. China

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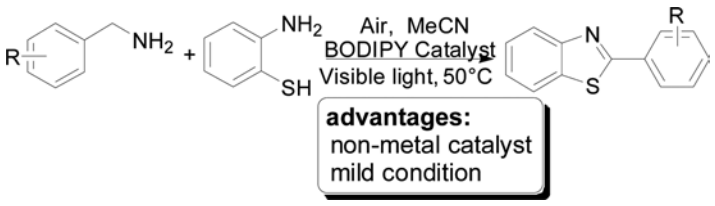
Syntheses of 2-Aryl Benzothiazoles via Photocatalyzed Oxidative Condensation of Amines with 2-Aminothiophenol in the presence of BODIPY Derivatives

Zeyin Zhou[1], Weijun Yang[1]

[1]Department of Chemistry and Chemical Engineering, Hunan University, Changsha, Hunan Province, P. R. China

Abstract

A simple, convenient, efficient and new method for synthesis of 2-Aryl benzothiazoles under a mild condition with non-metal catalyst has been developed. BODIPY dyes were used as photocatalyst for aerobic oxidative reactions of amine with 2-aminothiophenol. The approach will be very useful for the synthesis of benzothiazole derivatives and the development of photocatalytic reactions.



KEYWORDS: synthesis; benzothiazoles; BODIPY; photocatalysis; oxidation

INTRODUCTION

2-Aryl benzothiazoles play a very important role as organic functional materials in chemistry and are also widely used as biologically active products,[1,2] as well as marketed drugs or drug candidates.[3] For example, 2-Aryl benzothiazoles are not only

important fluorescent dyes that are used in fibre and plastic,[4] but also as liquid crystals and off-color material.[5,6] In medicine, 2-aryl benzothiazoles serve as fungicide,[7] acaricide,[8] and anticancer.[9]

Some synthesis methods for 2-aryl benzothiazoles have been reported in the literature.[10–17] Classic methods for the synthesis involve the condensation of 2-aminothiophenols with aryl aldehydes,[10] acyl chlorides,[11] carboxylic acids,[12] alcohols,[13] and amines[14] in the presence of oxidants. Another method is intramolecular cyclization reaction of *N*-(2-bromophenyl)benzothioamide with the Pd complex as catalyst. Moreover, it also has been demonstrated that 2-aryl benzothiazoles can be synthesized efficiently *via* transition-metal-catalyzed (Ni, Pd) cross-couplings between benzothiazoles and aryl halides,[15] aryl boronic acids,[16] or aromatic carboxylic acids.[17] Unfortunately, so many disadvantages, such as rigorous conditions (i.e. high temperature, long reaction time, and high pressure), hazardous oxidants,[18] or potential toxicity and high cost of the metal catalysts, presented in the above synthetic reactions, result in these transformations uneconomical and unfriendly to environment. Therefore, a new method for its construction is highly desirable.

With the demand for green chemistry, visible-light-responsive photoredox reactions show much prominence for the use of the visible light which is a clean energy source provided by the solar irradiance. BODIPY (boron-dipyrromethene) is a class of novel fluorescent

dyes. It is composed of dipyrromethene complexes with a substituted boron atom, typically a BF_2 unit.[19,20] Currently, BODIPY has been used as visible-light-responsive photocatalyst applied in oxidation of thioanisole and dihydroxylnaphthalenes,[21,22] which shows excellent photocatalytic activity. In these reactions, oxygen/air was used as the terminal oxidant. Mild condition and metal-free photoredox reaction driven by the BODIPY photosensitizer seems to be highly economical for their excellent properties such as strong fluorescence and absorption. Meanwhile, the molecular structure of BODIPY can be so easily tuned by a way of small modifications that we can choose a better catalyst to photocatalyze oxidative reaction. In this context, one-pot synthesis of 2-aryl benzothiazoles via BODIPY photocatalyzed oxidation of amines with 2-aminothiophenol in visible light was explored.

RESULTS AND DISCUSSION

There are several BODIPY photocatalysts prepared in this paper. As shown in Scheme 1, BODIPY **1** are made from aldehyde as electrophilic component to form the methane bridge between two pyrrole units. Then BODIPY **2** and BODIPY **3** are synthesized by using copper (II) bromide as bromination reagents in mild conditions with excellent yields and selectivity. Their structures are confirmed by the ^{1}H NMR, ^{13}C NMR and MS spectra. With BODIPYs in hand, we further studied the photophysical properties of these compounds. BODIPYs are colorful to our eyes, and most of them are brilliant upon

irradiation. UV-vis absorption and fluorescence spectra of BODIPYs were studied (see Figure 1).

BODIPYs' spectra show the typical narrow absorption and sharp fluorescence emission bands of classic difluoroboron dipyrrins, and the max fluorescence emission band (BODIPY **3b**, the blue dash line in Figure 1) can approach 580 nm, which displays near-IR emission. With the increased conjugation on BODIPY b moleculer, the spectra are red-shifted (10 nm for absorption and 10 nm for fluorescence emission) compared with those of BODIPY **a**. Meanwhile, with the increase of the amount of bromine atom in the BODIPY structure, obvious red-shifts of the absorption and emission was observed in BODIPY **3a**, and the Stokes shift are 10 nm and 20 nm respectively compared with BODIPY **1a** and BODIPY **2a**. On the other hand, fluorescence quantum yield was weakened to a great extent for this reason (see Table 1).

To solve the problems occurred in synthesis of 2-aryl benzothiazoles mentioned above, one-pot synthesis of 2-aryl benzothiazoles via BODIPY photocatalyzed oxidation of amines with 2-aminothiophenol in visible light was explored. We are aimed at accomplishing the transformation effectively under a mild condition with non-metal catalyst.

Results of control experiments and optimization of reaction conditions for the oxidation of benzylamine are shown in Table 2. Initially, the reaction was conducted without visible light (Table 2, entry 6), no product was detected in GC. Similarly, no transformation occurred in the absence of oxygen even with longer reaction time to 8h (Table 2, entry 5). When the reaction was conducted under light without BODIPY catalyst, no product was observed either (Table 2, entry 7). Meanwhile, we also found the mounts of 2-aminothiophenol (from 2 eq to 3 eq) and the reaction atmosphere (air to O_2) just have a slight effect to the reaction results, for the yields only rise 2 percent and 3 percent respectively. Therefore, the conclusion was made as follows: the light, photosensitizer and oxygen are essential to the photocatalytic oxidation. Subsequently, a better yield (80%) was obtained with temperature rising to 50 $^{\circ}$C (Table 2, entry 4). We further raised the reaction temperature to 80 $^{\circ}$C (Table 2, entry 10), GC shows that more side products were generated (the main side product is benzaldehydes). Changing the photosensitizer, however, compared with BODIPY **1** and BODIPY **2,** it is obvious that BODIPY **3** presents significant influences in the aerobic oxidation of benzylamine with 2-aminothiophenol at the same condition (Table 2, entry 1-3). The more the amount of bromine in the BODIPY structure, the better yield was obtained, which may suggest that bromine can promote the generation of $^1O_2$ in accordance with some reported results that the bromine substituted BODIPY extremely promoted the generation of $^1O_2$.[23,24] Based on these results, we decided to set heating the benzylamine and 2-aminothiophenol at

50 °C in the presence of BODIPY **3a** irradiated by a 35 W xenon lamp as our optimized condition.

With the optimized protocol results in hand, a number of experiments were carried out to explore the scope and limitation of the reaction (Table 3). We found that the reaction worked very well for a wide variety of substituted benzylamines, obtaining the expected substituted benzothiazoles in yields ranging from 42 to 81%. With various substituents such as methyl, chloro, fluoro, bromine, methoxy as well as naphthyl, all groups proceeded smoothly in good yields. For example, benzylamines substituted with electron-donating groups (CH_3 and OCH_3) (Table 3, entry 3, 4, 11), afford the target products in 78-81% yields; Halogen, such as chloro, bromine (Table 3, entry6, 9, 10) gives no problem, no matter for *para*-substituted benzylamines, *meta* or *ortho*, except the fluoro (Table 3, entry 2, 7), which are strong electron-withdrawing groups and only undergo the oxidative condensation with 42% yields. So the oxidation of the electron-donating groups proceeded more efficiently than the electron-withdrawing groups. We also found that no reaction occurred when amine lacking of α-H, such as aniline (Table 3, entry 15). Heterocyclic amine, such as thiophen-2-ylmethanamine, also proceeded smoothly with better yield.

Based on foregoing results, we proposed a mechanism that it is highly likely that the presence of singlet oxygen ($^1O_2$)[25] is responsible for the photooxidation of benzylamine

with 2-aminophenol. We further studied the influence of DABCO (1, 4-diazabicyclo[2.2.2]octane, a singlet oxygen scanvenger) to the oxidation. We found that the photocatalytic reaction can be significantly quenched by the DABCO. Therefore, we think $^1O_2$ is involved in the photooxidative process. The proposed mechanism was shown in Scheme 2. First, BODIPY accepted a photon from the visible light to form BODIPY* under the irradiation by visible light. Then, benzylamine was oxidized to form phenylmethanimine by singlet oxygen generated by energy transfer from BODIPY*. Finally, 2-aryl benzothiazole was formed by the condensation of intermediate. Some details about the singlet oxygen involved in the photosensitized oxidation reaction had been reported and discussed.[26,27] In terms of the energy requirements, BODIPY dyes generating singlet oxygen from the *triplet* excited state have been used in photodynamic therapy.[28–30]

In summary, several BODIPY dyes were synthesized, and their structures were confirmed by ^{1}H NMR, ^{13}C NMR, and MS spectra, and they were used as photocatalysts for aerobic oxidative reactions of amine with 2-aminothiophenol. A new method to synthesize 2-aryl benzothiazoles under a mild condition with a metal-free procedure using BODIPY as photocatalysts was developed. Our approach will be very useful for the synthesis of benzothiazoles derivatives and the development of photocatalytic reactions.

EXPERIMENTAL

General Procedure For BODIPY 1

Aryl-aldehyde (2.0 mmol), 2,4-dimethylpyrrole (423 mg, 4.5 mmol) were dissolved in (100 mL) absolute CH_2Cl_2. Trifluoroacetic acid (one drop) was added in the solution under argon. After the reaction mixture was stirred about 4 hours at room temperature until TLC-control showed the complete consumption of the aldehyde. Then DDQ (2,3-Dichloro-5,6-dicyano-1,4-benzoquinone) (454 mg, 2.0 mmol) in CH_2Cl_2 (50 mL) was added. The mixture was stirred for 30 min followed by the addition of Et_3N (6 mL) and $BF_3{\cdot}Et_2O$ (4 mL) at ice-cold condition and further stirred at room temperature for 3h. The reaction mixture was washed with water (3×100 mL), then the organic layer were combined and dried over with anhydrous $MgSO_4$ and evaporated to dryness. The crude product was further purified using column chromatography.

General Procedure For BODIPY 2

1,3,5,7-tetramethyl-BODIPY ***1*** (0.2 mmol) and K_2CO_3 (0.6 mmol) were dissolved in MeCN (20 mL). $CuBr_2$ (0.3 mmol) in MeCN (25 mL) was slowly added in the solution under an O_2 atmosphere (balloon). The mixture was stirred at r.t. for 24 h. The reaction mixture was washed with EtOAc (3×40 mL), and then washed with H_2O (3x30 mL). The organic layer were combined and dried over with anhydrous $MgSO_4$ and evaporated to dryness. The crude product was further purified using column chromatography.

General Procedure For BODIPY 3

*1,3,5,7-tetramethyl-BODIPY **1*** (0.2 mmol) and $CuBr_2$ (0.5 mmol) were dissolved in MeCN (20 mL) under an O_2 atmosphere (balloon). The mixture was stirred at r.t. for 12 h. The reaction mixture was washed with EtOAc (3×40 mL), and then washed with H_2O (3×30 mL). The organic layer were combined and dried over with anhydrous $MgSO_4$ and evaporated to dryness. The crude product was further purified using column chromatography.

Typical Procedures For Photocatalytic Oxidation Of Amine With 2-Aminothiophenol

To a dry 10 mL flask were added amine (1 mmol), 2-aminothiophenol (2mmol), *BODIPY photosensitizer* (0.01mmol, 1.0 mol %,) and acetonitrile(5 mL). The flask was pressurized with air (2 bar), and then heated to 50°C. The solution was then irradiated using a 35 W xenon lamp through a cut off filter (0.72 M $NaNO_2$ aqueous solution, which is transparent for light > 385 nm, because lamps could emit a small amount of ultraviolet light). After the reaction is completed, the solvent was evaporated under reduced pressure. The crude product was further purified using column chromatography.

SUPPORTING INFORMATION

Supplemental data for this article can be accessed on the publisher's website.

REFERENCES

1. (a) Chen, C. P.; Chen, Y. J. *Tetrahedron Lett*. **2004**, *45*, 113-115; (b) Alamgir, M.; Black, D. S. C.; Kumar, N. *Top. Heterocycl. Chem*. **2007**, *9*, 87-118.

2. Jain, A. K.; Paul, A.;Maji, B.; Muniyappa,K.; Bhattacharya, S. *J. Med. Chem*. **2012**, *55*, 2981-2993.

3. (a) Chen, Y. X.; Qian, L. F.; Zhang, W.; Han, B. *Angew. Chem*. **2008**, *120*, 9470-9473; (b) Shiraishi, Y.; Sugano, Y.; Tanaka, S.; Hir*ai*, T. *Angew. Chem*. **2010***, 122*, 1700-1704.

4. Chevrie, D.; Lequeux, T.; Demoute, J. P.; P*azenok, S. Tetrahedron, Lett*. **2003**, *44*, 8127-8130.

5. (a) Nakamura, S.; Takiguchi, T.; Tokano, G.; Kosaka, Y.; *JP 08157397,* **1996** [*Chem Abstr*. 1996, 125. 208567x]; (b) Nakamura, S.; Takiguchi, T.; Tokano, G.; Kosaka, Y.; *JP 08157398,* **1996** [*Chem Abstr*. 1996, 125. 208568y].

6. Heynderickx, A.; Guglielmetti, R.; Dubest, R.; Aubard, J.; Samat, A.; *Synthesis.* **2003**, 1113-1117.

7. Mathews, C. J.; Banett, S. P.; Smith, S. C. *WO 0006566*. **2000** [*Chem Abstr*. 2000, *132*. 151818t].

8. Moury, T.; Tokumura, J.; Kochi, S.; Fukui, H.; Nakano, J.; Ando, T. *Nippn Noyau Gkkaishi.* **2002**, *27*, 353-356.

9. (a) Stevens, M. F. G.; Shi, D. F.; Castro, A. *J. Chem. Soc., Perkin Trans*. *1*. **1996**, 83-93; (b) Hutchinson, I.; Chua, M. S.; Browne, H. L.; Trapani, V. *J. Med. Chem*. **2001**, *44*, 1446-1455.

10. (a) Parikh, N.; Kumar, D.; Roy, S. R.; Chakraborti, A. K. *Chem.Commun*. **2011**, *47*, 1797-1797; (b) Bahrami, K.; Khodaei, M. M.; Naali, F. *J. Org. Chem*. **2008**, *73*, 6835-6837; (c) Yang, Z. Y.; Chen, X.; Wang, S. Z.; Liu, J. D.; Xie, K.; Wang, A. W.; Tan, Z. *J. Org. Chem.* **2012**, *77*, 7086-7091.

11. (a) Nadaf, R. N.; Siddiqui, S. A.; Thomas, D.; Lahoti, R. J.;Srinivasan, K. V. *J. Mol. Catal. A: Chem*. **2004**, *214*, 155-160; (b) Rudrawar, S.; Kondaskar, A.; Chakraborti, A. K. *Synthesis.* **2005**, *15*, 2521-2526.

12. (a) Sharghi, H.; Asemani, O. *Synth. Commun*. **2009**, *39*, 860-867; (b) Deligeorgiev, T. G. *Dyes Pigments.* **1990**, *12*, 243-248.

13. Wilfred, C. D.; Taylor, R. J. K. *Synlett.* **2004**, *9*, 1628-1630.

14. (a) Thanh, B. N.; Ludmila, E.; William, A. D. *Org Let.* **2012**, *14*(23), 5948-5951; (b) Su, F. Z.; Smitha, C; Mathew; Lennart, M.; Markus, A.; Wang, X. C.; Siegfried, B. *Angew. Chem. Int. Ed*. **2011**, *50*, 657-660; (c) Yang, Z.Y.; Wang, A.W.; Chen, X.; Gui, Q. W.; Liu, J. D.; Tan, Z.; Wang, H.; Shi, J. C. *Synlett.* **2013**, *24*, 1549-1554.

15. (a) Shibahara, F.; Yamaguchi, E.; Murai, T. *Chem. Commun.* **2010**, *46*, 2471-2473; (b) Canivet, J.; Yamaguchi, J.; Ban, I.; Itami, K. *Org. Lett.* **2009**, *11*, 1733-1736.

16. (a) Ranjit, S.; Liu, X. *Chem. Eur. J.* **2011**, *17*, 1105-1108; (b) Guchhait, S. K.; Kashyap, M.; Saraf, S. *Synthesis.* **2010**, 1166-1170.

17. Zhang, F.; Greaney, M. F. *Angew. Chem. Int. Ed.* **2010**, *49*, 2768-2771.

18. (a) Altenhoff, G.; Glorius, F. *Adv. Synth. Catal.* **2004**, *346*, 1661-1664; (b) Evindar, G.; Bartey, R. A. *J. Org. Chem.* **2006**, *71*, 1802-1808.

19. Jiao, L. J.; Yu, C.; Li J.; Wang, Z.; Wu, M.; Hao, E. *J. Org. Chem.* **2009**, *74*, 525-528.

20. Ye, J. H.; Wang, G. P.; Huang, C. M.; Hu, Z. J.; Zhang, W. C. Zhang Y. *Synthesis.* **2012**, *44*, 104-110.

21. Li, W. L.; Xie, Z. G.; Jing, X. B. *Catal Commun.* **2011**, *16*, 94-97.

22. Yang, P.; Zhao, J. Z.; Wu, W. H.; Yu, X. R.; Liu, Y. F. *J. Org. Chem.* **2012**, *77*, 6166-6178.

23. Nagappanpillai, A.; Rekha, R. A.; Danaboyina, R. *Org. Lett.* **2010**, *12*, 5720-5723.

24. Bunton, C. A.; Gillitt, N. D. *J. Phy. Org. Chem.* **2002**, *15*, 29-35.

25. Acquaye, J. H.; Muller, J.G.; Takeuchi, K. J. *Inorg Chem.* **1993**, *32*, 160-165.

26. Foote, C. S.; Wexler, S. *J. Am. Chem. Soc.* **1964**, *86*, 3880-3881.

27. Corey, E. J.; Taylor, W. C. *J. Am. Chem. Soc.* **1964**, *105*, 3881-882.

28. Yogo, T.; Urano, Y.; Ishitsuka, Y.; Maniwa, F.; Nagano, T. *J. Am. Chem. Soc.* **2005**, *127*, 12162-12163.

29. Atilgan, S.; Ekmekci, Z. Dogan, A. L.; Guc, D.; Akkaya, E. U. *Chem Comm.* **2006**, *42*, 4398-4400.

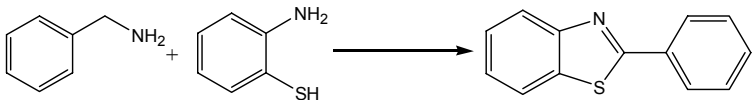
30. Lai,Y. C.; Su, S. Y.; Chang, C. C. *Appl. Mater. Interfaces*. **2013**, *5*, 5931-5936.

Table 1. Photophysical Properties of BODIPYs in Dichloromethane*

BODIPY	λmax/nm	λ_f/nm	Δλ/nm	ε/10^5M^{-1}cm^{-1}	Φ_f
1a	502	521	19	0.64	0.61
2a	510	533	23	0.58	0.12
3a	528	551	23	0.57	0.08
1b	510	530	20	0.70	0.76
2b	518	540	22	0.62	0.15
3b	538	570	32	0.59	0.11

*With fluorescein as the standard (Φ_f= 0.85 in NaOH).

Table 2. Reaction Condition Optimization



Entry	photosensitizer	condition	T/°C	T/h	Yield/%[b]
1	BODIPY **1a**/**1b**	In air	23	5	24/22
2	BODIPY **2a**/**2b**	In air	23	5	31/28
3	BODIPY **3a**/**3b**	In air	23	5	40/36
4	**BODIPY 3a**	**In air**	**50**	**5**	**80**
5	BODIPY **3a**	In N_2	50	10	--[e]
6[c]	BODIPY **3a**	In air	50	5	--
7	No catalyst	In air	50	5	--
8[d]	BODIPY **3a**	In air	50	5	82
9	BODIPY **3a**	In O_2	50	5	83
10	BODIPY **3a**	In air	80	5	73

[a]Reaction conditions:benzylamine (1mmol), 2-aminothiophenol (2eq, 2 mmol), photosensitizers catalyst (1 mol%), acetonitrile as solvent (5 mL), $\lambda > 380$ nm, P=0.20MPa.

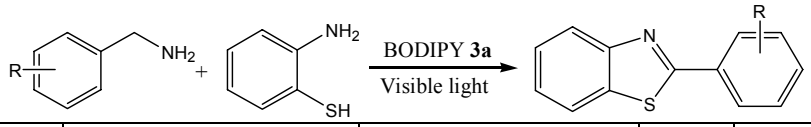
[b]Yield are determined by GC.

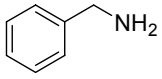
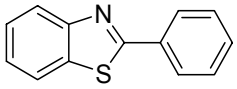
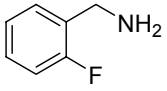
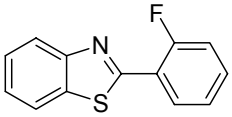
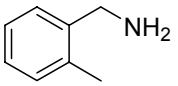
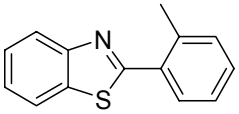
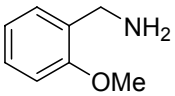
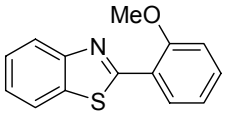
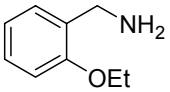
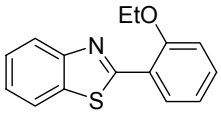
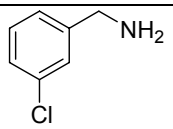
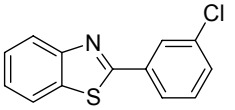
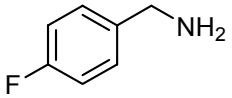
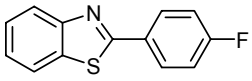
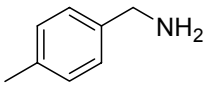
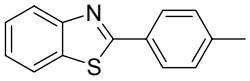
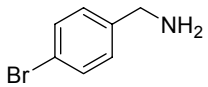
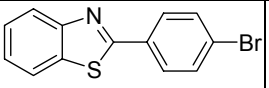
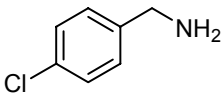
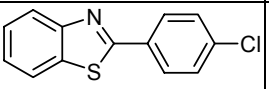
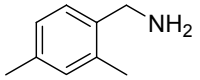
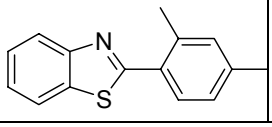
[c]No photo-irradiation.

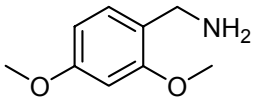
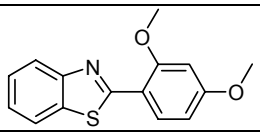
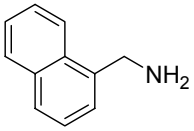
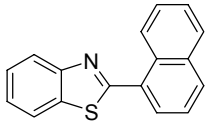
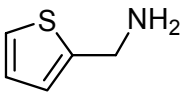
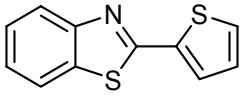
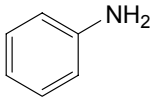
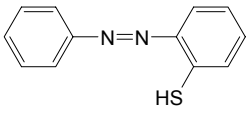
[d]2-aminothiophenol (3 eq, 3 mmol).

[e]No reaction.

Table 3. Oxidation of various substituted amines using BODIPY **3a**



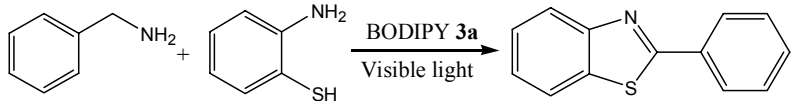
Entry	Substrate	Product	T/h	Yield/%[b]
1			5	80
2			5	42
3			5	81
4			5	78
5			5	76
6			5	72
7			5	49
8			5	69
9			5	75
10			5	74
11			5	79

12			5	78
13			5	76
14			5	81
15			5	0

[a]Reaction conditions:amine (1mmol), 2-aminothiophenol (2 eq, 2 mmol), BODIPY **3a** (1 mol%), acetonitrile as solvent (5 mL), $\lambda > 380$ nm, T=50°C, in air P=0.20 MPa.

[b]Isolated yield based on amine.

Table 4. Mechanism study of the oxidative experiments

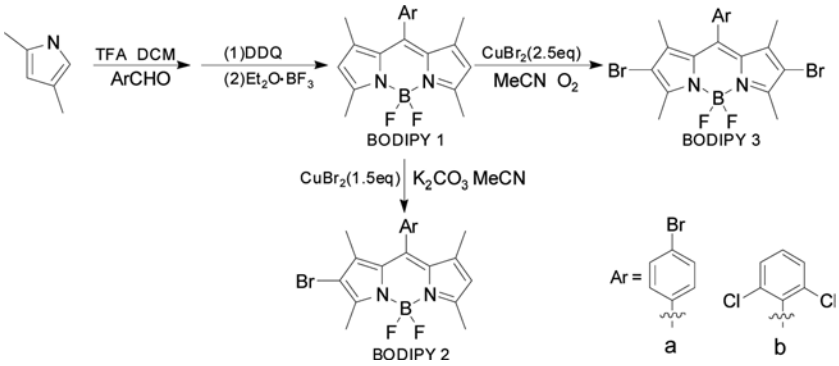


Entry	Add DABCO%	Yield %[b]
1	0	80
2	2	35
3	5	0

[a]Reaction conditions: benzylamine (1 mmol), 2-aminopheno (2 mmol), photosensitizers catalyst (1 mol%), acetonitrile (5 mL), in air P=0.2 MPa, λ> 380 nm, 50°C.

[b]Yield was determined with GC.

Scheme 1. Synthesis of BODIPYs.



Scheme 2. Proposed reaction mechanism for the photocatalytic aerobatic oxidation with the photosensitizer BODIPY **3a**

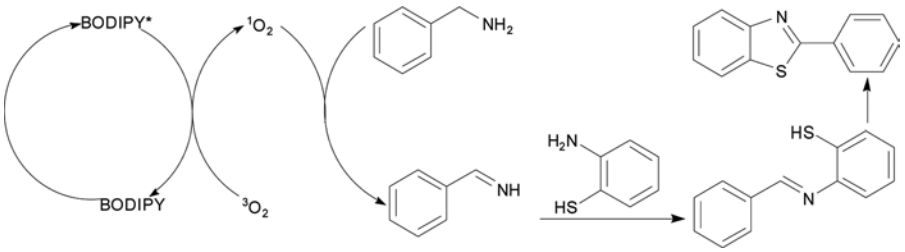


Figure 1. Steady state UV−vis absorption (solid line) and fluorescence (dash line) spectra measured in dichloromethane.