

Direct *meso*-Amidation of Biellmann BODIPY [†]

 Alexis S. Zamora-Vázquez ¹, Miguel A. Vázquez ¹, José L. Belmonte-Vázquez ² and Eduardo Peña-Cabrera ^{1,*}
¹ Departamento de Química, Universidad de Guanajuato, Noria Alta S/N, Guanajuato 36050, Mexico; as.zamoravazquez@ugto.mx (A.S.Z.-V.); mvazquez@ugto.mx (M.A.V.)

² Departamento de Química Orgánica, Facultad de Química (FQ), Universidad Nacional Autónoma de México (UNAM), Ciudad Universitaria, Ciudad de México 04510, Mexico; jl.belmonte@quimica.unam.mx

* Correspondence: eduardop@ugto.mx

[†] Presented at the 30th International Electronic Conference on Synthetic Organic Chemistry, 5–19 November 2026; <https://sciforum.net/event/ecsoc-30/home>.

Abstract

This work represents the first-ever *meso*-direct incorporation of borodipirromethenes to amide-containing molecules throughout Biellmann BODIPY by *meso*-functionalization. The present study employs the well-known ability of the -SMe group as a salient group in a novel reactivity fashion with amides as a reaction partner in the presence of K₂CO₃, CuTC and the catalytic system of CuI/phen in sustainable 2-MeTHF/H₂O at 90 °C to afford 16 derivatives of *meso*-amidoBODIPYs in a yield range of 12 to 67% in 2.5 to 24 h of reaction time.

Keywords: BODIPY; amide-fluorescent labeling; copper catalysis

1. Introduction

Amides are one of the most characteristic functional groups in chemistry. In general, amides are well-known for their increased stability in the N-acyl bond and low nucleophilicity of nitrogen. Moreover, around 25% of commercially available drugs contain an amide functional group [1]. Also, we can find amides in peptides, materials, agrochemicals, natural products, etc. Derivatization of fluorophores as cyanines, coumarins or BODIPYs has emerged as an important field in the creation of novel materials because of its application in biomedical sciences. In that sense, structural modification around the BODIPY core has been studied because simple modification can cause a fluorogenic response [2].

The seminal work of Saucedo et al. discusses *meso*-amidoBODIPY synthesis, employing BODIPY amino-derivative treatment with NaH and acyl chlorides to afford an amide derivative. Since then, similar reactivity fashions have been reported for the creation of these types of compounds, but by this manner, they could not be labeled preformed amides [3].

Typical ways for amide *N*-arylation had been studied by Ullmann, Goldberg, Buchwald, Hartwig and Ma by using Cu, Pd and Ni catalysis between aryl halide and amides as reaction partners [4]. In that sense, Peña-Cabrera has reported the use of *meso*-methylsulfanylBODIPY, the Biellmann BODIPY, in cross-coupling Pd-catalyzed Liebeskind-Srogl or Sonogashira reaction [5,6]. So, in this work, we present the first attempt of the application of the Ullmann–Goldberg *N*-arylation type-reaction for *meso*-amideBODIPY synthesis using the Biellmann BODIPY heterocycle as a synthetic fluorescent platform and amide-containing molecules in the presence of catalytic system CuI/phen in a sustainable 2-MeTHF/H₂O solvent system at 90 °C as shown in Scheme 1.



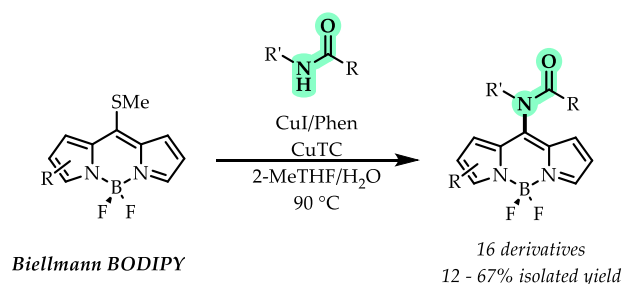
Academic Editor: Julio A. Seijas

Published: 21 October 2026

Copyright: © 2026 by the authors.

Licensee MDPI, Basel, Switzerland.

 This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC BY\)](https://creativecommons.org/licenses/by/4.0/) license.



Scheme 1. Overview of the present work.

2. Materials and Methods

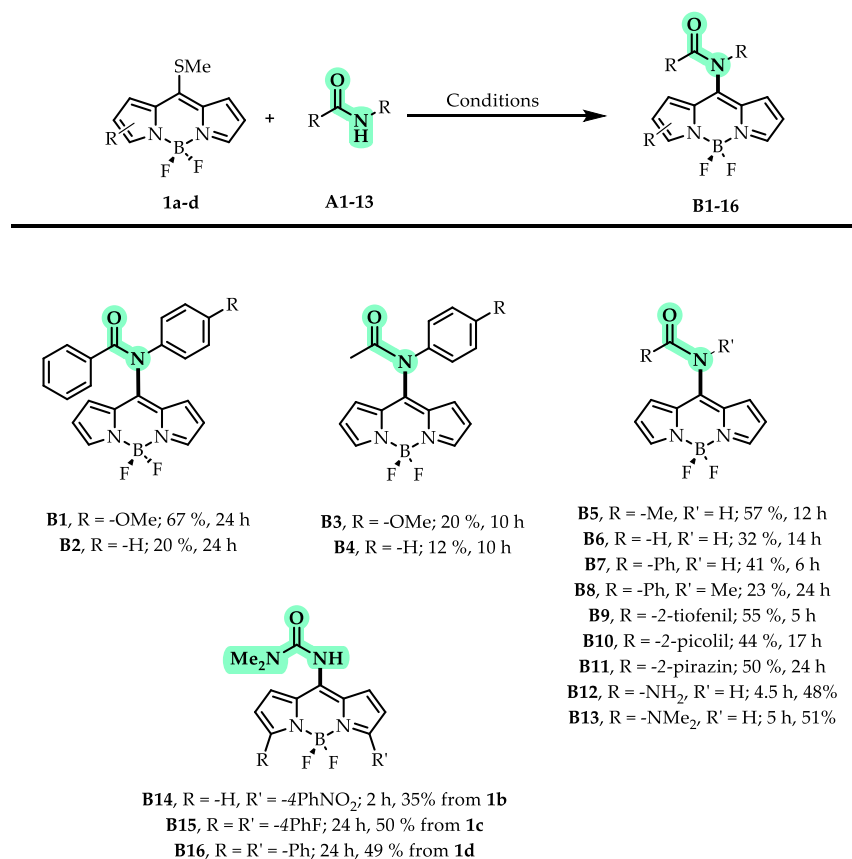
The starting materials and reagents were commercially available at Sigma-Aldrich website unless otherwise stated. Solvents were distilled and dried by standard procedures. Reactions were carried out in oven- or flame-dried glassware, without an inert atmosphere unless noted. Progress was monitored by TLC on silica gel F-254 (Merck, Darmstadt, Germany) under UV (254/365 nm). Flash chromatography was performed on silica gel Kieselgel 60 (70–230 mesh) with hexanes/ethyl acetate mixtures. HRMS samples were ionized by ESI+ and recorded via the TOF method. Biellmann BODIPY derivatives were purchased from Cuántico de México (Guanajuato, Mexico).

3. Results

First of all, *N*-(*p*-methoxyphenyl)benzamide was selected as the standard amide for trying to obtain amidation product **B1** with Biellmann BODIPY as the reaction partner. After several essays, *meso*-amidoBODIPY **B1** was obtained in 67% isolated yield after 24 h by treatment with CuI and phenanthroline, K₂CO₃ and copper (I) 2-thiophenecarboxylate in a 2-MeTHF/H₂O system at 90 °C.

With this result in hand, we now focused on implementing the new method to a series of structurally simple amides for the synthesis of a series of *meso*-amidoBODIPYs **B1–16**. Some of those products were structurally modified Biellmann BODIPYs under the aforementioned reaction conditions. The products **B1–16** were obtained in a range of 12 to 67% isolated yield after 2.5 to 24 h. The reaction conditions were applied to secondary amides derived from *N*-phenyl benzamide **A1–2**, *N*-phenyl acetamides **A3–4**, and one example of *N*-alkyl benzamide **A8**, and primary amides as acetamide **A5**, formamide **A6**, benzamide **A7**, heterocyclic carboxamides derived from thiophene, pyridine and pyrazine **A9–11** and a pair of urea derivatives **A12–13**. The results show reduced reaction times in the coupling of primary amides rather than those for secondary amides. Also, isolated yields for secondary amides have almost generally reduced values. In direct comparison with this observation, benzamide **A7** afforded coupled product **B7** in 41% after 6 h. On the other hand, *N*-methyl benzamide **A8** illustrates a drastically increased reaction time for obtaining the corresponding product **B8** with a notably decreased yield of 23%. The synthesis of **B12–13** derivatives demonstrates significantly reduced reaction times and yields around 50%.

In the case of the structurally modified Biellmann BODIPYs, the new reaction was applied to 3-aryl nor 3,5-diaryl BODIPYs **1b–d** with amide **A13**. For the 3-(4-nitrophenyl)-8-methylsulfanylBODIPY **1b** amidation case, the reaction time was reduced by the -NO₂ electron-withdrawing group; despite this modification, the isolated yield was around 35%. In the case of **1c–d**, the diaryl modification denotes an increase in the reaction time but did not affect yield compared with **B13** synthesis. Products **B15–16** yield around 50%. Summarized results are presented in Scheme 2.



Scheme 2. Scope of direct-*meso* amidation of Biellmann BODIPYs **1a-d** by amide-containing molecules **A1-13**.

The present work is currently under development, so the physicochemical properties and optical features of **B1-16** are not presented.

4. Conclusions

In this report, we present the preliminary results of the first attempt of synthesis of *meso*-amidoBODIPYs by direct incorporation of amide-containing compounds to the *meso* carbon of BODIPY employing *meso*-methylsulfanylbODIPY, the Biellmann BODIPY, as a synthetic platform in an Ullmann–Goldberg approach by the use of a copper (I)/diamine catalytic system in a sustainable mixture of 2-MeTHF/water at 90 °C.

5. Compounds Characterization

B1. HRMS-TOF (ESI+): m/z calculated for C₂₃H₁₈BF₂N₃O₂ [M + NH₄]⁺, 435.1839, found 435.1802.

B2. HRMS-TOF (ESI+): m/z calculated for C₂₂H₁₆BF₂N₃O [M + H]⁺, 388.1442, found 388.1431.

B3. HRMS-TOF (ESI+): m/z calculated for C₁₇H₁₄BF₂N₃O [M + H]⁺, 326.1290, found 326.1274.

B4. HRMS-TOF (ESI+): m/z calculated for C₁₈H₁₆BF₂N₃O₂ [M + H]⁺, 356.1398, found 356.1380.

B6. HRMS-TOF (ESI+): m/z calculated for C₁₀H₈BF₂N₃O [M + H]⁺, 236.0807, found 236.0810.

B8. HRMS-TOF (ESI+): m/z calculated for C₁₇H₁₄BF₂N₃O [M + H]⁺, 326.1296, found 326.1274.

B9. HRMS-TOF (ESI+): m/z calculated for $C_{14}H_{10}BF_2N_3OS$ $[M + H]^+$, 318.097, found 318.081.

B12. HRMS-TOF (ESI+): m/z calculated for $C_{10}H_9BF_2N_4O$ $[M + Na]^+$, 273.0735, found 273.0756.

B13. HRMS-TOF (ESI+): m/z calculated for $C_{12}H_{13}BF_2N_4O$ $[M + Na]^+$, 301.1058, found 301.1045.

B14. HRMS-TOF (ESI+): m/z calculated for $C_{18}H_{16}BF_2N_5O_3$ $[M + H]^+$, 400.1406, found 400.1390.

B15. HRMS-TOF (ESI+): m/z calculated for $C_{24}H_{19}BF_4N_4O$ $[M + H]^+$, 467.1680, found 467.1665.

B16. HRMS-TOF (ESI+): m/z calculated for $C_{24}H_{21}BF_2N_4O$ $[M + H]^+$, 430.1776, found 430.1780.

Author Contributions: Conceptualization, E.P.-C.; methodology, A.S.Z.-V.; validation, A.S.Z.-V., M.A.V., J.L.B.-V. and E.P.-C.; formal analysis, A.S.Z.-V., M.A.V., J.L.B.-V. and E.P.-C.; investigation, A.S.Z.-V.; resources, E.P.-C.; data curation, E.P.-C.; writing—original draft preparation, A.S.Z.-V.; writing—review and editing, E.P.-C.; visualization, E.P.-C.; supervision, M.A.V., J.L.B.-V. and E.P.-C.; project administration, E.P.-C.; funding acquisition, E.P.-C. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by DAIP-UG (grant #076-2025 and #226/2026).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The datasets presented in this article are not readily available. Requests to access the datasets should be directed to E.P.-C.

Acknowledgments: A.S.Z.-V. wish to thank SECIHTI (Mexico) for a graduate scholarship. The authors appreciate the Guanajuato National Laboratory UG-UAA-CONACyT (# 316011) for their generous allocation of analytical resources.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

BODIPY	Borodipirromethene
-SMe	Methylsulfanyl substituent
CuTC	Copper (I) 2-thiophenecarboxylate
K_2CO_3	Potassium Carbonate
CuI	Copper Iodide
Phen	Phenanthroline
2-MeTHF	2-methyl tetrahydrofuran
NaH	Sodium Hydride
UV	Ultraviolet light

References

1. Ojeda-Porras, A.; Gamba-Sánchez, D. Recent Developments in Amide Synthesis Using Nonactivated Starting Materials. *J. Org. Chem.* **2016**, *81*, 11548–11555. [[CrossRef](#)] [[PubMed](#)]
2. Ulrich, G.; Ziesse, R.; Harriman, A. The Chemistry of Fluorescent Bodipy Dyes: Versatility Unsurpassed. *Angew. Chem. Int. Ed.* **2008**, *47*, 1184–1201. [[CrossRef](#)] [[PubMed](#)]
3. Shi, W.; Li, J.; He, X.; Zhou, S.; Sun, H.; Wu, H. Tuning the Physicochemical Properties of BODIPY for Bioimaging via meso-Amino Acylation. *Org. Lett.* **2022**, *24*, 3368–3372. [[CrossRef](#)] [[PubMed](#)]

4. Morrison, K.M.; Stradiotto, M. Advances in Copper and Nickel C–N and C–O Cross-Couplings of (Hetero)Aryl Chlorides Enabled by Ancillary Ligand Development. *Chem. Eur. J.* **2025**, *31*, e202501858. [[CrossRef](#)] [[PubMed](#)]
5. Yang, R.; Guan, H.; Jin, J.; Zheng, T.; He, L.; Zhang, Y.; Tian, L.; Wang, J.; Li, X. A Review on the Synthetic Methods for the BODIPY Core. *Compounds* **2025**, *5*, 42. [[CrossRef](#)]
6. Díaz-Rivera, M.d.R.J.; Turlakov, G.; Valenzuela-Soto, J.H.; Arias, E.; Moggio, I.; García-Muñoz, B.; Aguilar-Aguilar, A.; Vázquez, M.A.; Peña-Cabrera, E. Sonogashira-like Reaction of the Biellmann BODIPY and Fluorescence Staining of the Tomato Crop Bacterial Pathogen *Clavibacter michiganensis* with the Resulting Products. *Eur. J. Org. Chem.* **2025**, *28*, e202500601. [[CrossRef](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.