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Design, Spectral Characteristics, and Possibilities for Practical Application of BODIPY FL-Labeled Monoterpenoid

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Abstract

This article describes the design and biological properties of a BODIPY FL-labeled monoterpenoid BF2-meso-(4-((1″R)-6″,6″-dimethylbicyclo[3.1.1]hept-2″-ene-2″)yl-methoxycarbonylpropyl)-3,3′,5,5′-tetramethyl-2,2′-dipyrromethene conjugate (BODIPYmyrt). The fluorophore was characterized using X-ray, NMR, MS, and UV/vis spectroscopy. The conjugate exhibits a high quantum yield (to ~100%) in the region 515-518 nm. BODIPYmyrt effectively penetrates the membranes of the bacterial and fungal cells and therefore can be used to examine the features of a broad spectrum of Gram-positive and Gram-negative bacteria and pathogenic fungi as well. Moreover, BODIPYmyrt exhibits a moderate tropism to the subcellular structures in mammalian cells (e.g., mitochondria), thereby providing an attractive scaffold for fluorophores to examine these particular organelles.

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Keywords

(+)-myrtenol, biovisualization, BODIPY FL-labeled monoterpenoid, conjugate, spectral properties, structure

References

[1] Solomonov, A.; Marfin, Y.; Rumyantsev, E. Design and applications of dipyrrin-based fluorescent dyes and related organic luminophores: From individual compounds to supramolecular self assembled systems. Dyes Pigm. 2019, 162, 517-542, 10.1016/j.dyepig.2018.10.042

[2] Okamoto, M.; Kabayashi, S.; Ikeuchi, H.; Yamada, S.; Yamanouchi, K.; Nagasawa, K.; Maekawa, S.; Kato, T.; Shimizu, I. Synthesis and bioassay of a boron-dipyrromethene derivative of estradiol for fluorescence imaging in vivo. Steroids 2012, 77, 845-849, 10.1016/j.steroids.2012.04.011

[3] Jantra, S.; Butta, P.; Jithavech, P.; Rojsitthisak, P.; Palaga, T.; Rashatasakhon, P.; Sukwattanasilnitt, M.; Wacharasindhu, S. "Turn on" orange fluorescent probe based on styryl-BODIPY for detection of hypochlorite and its application in live cell imaging. Dyes Pigm. 2019, 162, 189-195, 10.1016/j.dyepig.2018.10.007

[4] West, R.; Panagabko, C.; Atkinson, J. Synthesis and characterization of BODIPY-α-tocopherol: a fluorescent form of vitamin E. J. Org. Chem. 2010, 75, 2883-2892, 10.1021/jo100095n

[5] Alekseeva, A.; Tretiakova, D.; Melnikova, D.; Molotkovsky, U. l.; Boldyrev, I. Novel fluorescent membrane probe 2,3,5,6-bis(cyclohexyl)-BODIPY-labeled phosphatidylcholine. Russ. J. Bioorg. Chem. 2016, 42, 305-309, 10.1134/S1068162016030031

[6] Kowada, T.; Maeda, H.; Kikuchi, K. BODIPY-based probes for the fluorescence imaging of biomolecules in living cells. Chem. Soc. Rev. 2015, 44, 4953-4972, 10.1039/C5CS00030K

[7] Gabe, Y.; Urano, Y.; Kikuchi, K.; Kojima, H.; Nagano, T. Highly sensitive fluorescence probes for nitric oxide based on boron dipyrromethene chromophores rational design of potentially useful bioimaging fluorescence probe. J. Am. Chem. Soc. 2004, 126, 3357-3367, 10.1021/ja037944j

[8] Guo, B.; Peng, X.; Cui, A.; Wu, Y.; Tian, M.; Zhang, L.; Chen, X.; Gao, Y. Synthesis and spectral properties of new boron dipyrromethene dyes. Dyes Pigm. 2007, 73, 206-210, 10.1016/j.dyepig.2005.11.007

[9] Chen, Y.; Wan, L.; Zhang, D.; Bian, Y.; Jiang, J. Modulation of the spectroscopic property of Bodipy derivates through tuning the molecular configuration. J. Photochem. Photobiol., C 2011, 10, 1030-1038, 10.1039/c1pp00001b

[10] Boldyrev, I.; Molotkovsky, J. Synthesis and properties of new 4,4-difluoro-3a,4a-diaza-s-indacene (BODIPY)-labeled lipids. Bioorg. Khim. 2006, 32, 78-83, 10.1134/S1068162006010080

[11] Guseva, G.; Antina, E.; Berezin, M.; Pavelyev, R.; Kayumov, A.; Sharafutdinov, I.; Lisovskaya, S.; Lodochnikova, O.; Islamov, D.; Usachev, K.; Boichuk, S.; Nikitina, L. Meso-substituted-BODIPY based fluorescent biomarker: spectral characteristics, photostability and possibilities for practical application. J. Photochem. Photobiol., A 2020, 401, 112783 10.1016/j.jphotochem.2020.112783

[12] Guseva, G.; Antina, E.; Berezin, M.; Lisovskaya, S.; Pavelyev, R.; Kayumov, A.; Lodochnikova, O.; Islamov, D.; Usachev, K.; Boichuk, S.; Nikitina, L. Spectroscopic and in vitro investigations of boron(III) complex with meso-4-methoxycarbonylpropylsubstituted dipyrromethene for fluorescence bioimaging applications. Molecules 2020, 25, 4541 10.3390/molecules25194541

[13] Oz, M.; Nebrisi, E.; Yang, K.; Howarth, F.; Kury, L. Cellular and molecular targets of menthol actions. Front. Pharmacol. 2017, 8, 472 10.3389/fphar.2017.00472

[14] Nikitina, L.; Kiselev, S.; Bodrov, A.; Startseva, V.; Artemova, N.; Klochkov, V.; Galiullina, L.; Aganova, O.; Khaliullina, A.; Lodochnikova, O. et al. Development of approaches to the study of the interaction of biologically active thioterpenoids with model membranes. BioNanoScience 2017, 7, 600-607, 10.1007/s12668-017-0432-0

[15] Nikitina, L.; Kiselev, S.; Startseva, V.; Bodrov, A.; Azizova, Z.; Shipina, O.; Fedyunina, I.; Boichuk, S.; Lodochnikova, O.; Klochkov, V. et al. Sulfur-containing monoterpenoids as potential antithrombotic drugs: research in the molecular mechanism of coagulation activity using pinanyl sulfoxide as an example. Front. Pharmacol. 2018, 9, 116 10.3389/fphar.2018.00116

[16] Nikitina, L.; Pavelyev, R.; Startseva, V.; Kiselev, S.; Galiullina, L.; Aganova, O.; Timerova, A.; Boichuk, S.; Azizova, Z.; Klochkov, V.; Huster, D.; Khodov, I.; Scheidt, H. Structural details on the interaction of biologically active sulfur-containing monoterpenoids with lipid membranes. J. Mol. Liq. 2020, 301, 112366 10.1016/j.molliq.2019.112366

[17] Mockute, D.; Judzentiene, A. Variability of the essential oils composition of Achillea millefolium ssp. millefolium growing wild in Lithuania. Biochem. Syst. Ecol. 2003, 31, 1033-1045, 10.1016/S0305-1978(03)00066-8

[18] Ngan, L.; Moon, J.; Shibamoto, T.; Ahn, Y. Growth-inhibiting, bactericidal, and urease inhibitory effects of Paeonia lactiflora root constituents and related compounds on antibiotic-susceptible and resistant strains of Helicobacter pylori. J. Agric. Food Chem. 2012, 60, 9062-9073, 10.1021/jf3035034

[19] Bhatia, H.; Sharma, Y.; Manhas, R.; Kumar, K. Ethnomedicinal plants used by the villagers of district Udhampur. J. Ethnopharmacol. 2014, 151, 1005-1018, 10.1016/j.jep.2013.12.017

[20] Cano-Ramírez, C.; Armendariz-Toledano, F.; Macias-Samano, J. E.; Sullivan, B.; Zúniga, G. Electrophysiological and behavioral responses of the bark beetle Dendroctonus rhizophagus to volatiles from host pines and conspecifics. J. Chem. Ecol. 2012, 38, 512-524, 10.1007/s10886-012-0112-z

[21] Lawal, O.; Oyedeji, A. Chemical composition of the essential oils of Cyperus rotundus L. from South Africa. Molecules 2009, 14, 2909-2917, 10.3390/molecules14082909

[22] Silva, R.; Salvadori, M.; Sousa, F.; Santos, M.; Carvalho, N.; Sousa, D.; Gomes, B.; Oliveira, F.; Barbosa, A.; Freitas, R.; Almeida, R.; Medeiros, J. Evaluation of the anti-inflammatory and antinociceptive effects of myrtenol, a plant-derived monoterpene alcohol, in mice. Flavours Fragrances 2014, 29, 184-192, 10.1002/ffj.3195

[23] Nikitina, L.; Startseva, V.; Dorofeeva, L.; Artemova, N.; Kuznetsov, I.; Lisovskaya, S.; Glushko, N. Antifungal activity of bicyclic monoterpenoids and terpenesulfides. Chem. Nat. Compd. 2010, 46, 28-32, 10.1007/s10600-010-9517-5

[24] Nikitina, L.; Startseva, V.; Vakulenko, I.; Khismatulina, I.; Lisovskaya, S.; Glushko, N.; Fassakhov, R. Synthesis and antifungal activity of compounds of the pinane series. Pharm. Chem. J. 2009, 43, 251-254, 10.1007/s11094-009-0282-3

[25] Cândido Moreira, M. R.; Salvadori, M.; Cardoso de Almeida, A.; Pergentino de Sousa, D.; Jordan, J.; Satyal, P.; Mendes de Freitas, R.; Nobregade Almeida, N. Anxiolytic-like effects and mechanism of (-)-myrtenol: a monoterpene alcohol. Neurosci. Lett. 2014, 579, 119-124, 10.1016/j.neulet.2014.07.007

[26] Yamamoto, Y.; Hosokawa, M.; Kurihara, H.; Maoka, T.; Miyashita, K. Synthesis of phosphatidylated-monoterpene alcohols catalyzed by phospholipase D and their antiproliferative effects on human cancer cells. Bioorg. Med. Chem. Lett. 2008, 18, 4044-4046, 10.1016/j.bmcl.2008.05.113

[27] Guseva, G.; Ksenofontov, A.; Antina, E.; Berezin, M.; Vyugin, A. Effect of solvent nature on spectral properties of blue-emitting meso-propargylamino-BODIPY. J. Mol. Liq. 2019, 285, 194-203, 10.1016/j.molliq.2019.04.058

[28] Roacho, R. I.; Metta-Magaña, A.; Portillo, M.; Peña-Cabrera, E.; Pannell, K. 8-Amino-BODIPYs: structural variation, solvent-dependent emission, and VT NMR spectroscopic properties of 8-RN-BODIPY. J. Org. Chem. 2013, 78, 4245-4250, 10.1021/jo302758a

[29] Kritskaya, A.; Berezin, M.; Antina, E.; Vyugin, A. Effect of aryl-, halogen-, and ms-aza-substitution on the luminescent properties and photostability of difluoroborates of 2,2′-dipyrrometenes. J. Fluoresc. 2019, 29, 911-920, 10.1007/s10895-019-02403-2

[30] Bumagina, N.; Antina, E.; Berezin, M.; Kalyagin, A. Influence of structural and solvation factors on the spectral-fluorescent properties of alkyl-substituted BODIPYs in solutions. Spectrochim. Acta, Part A 2017, 173, 228-234, 10.1016/j.saa.2016.09.026

[31] Chin, Y.; Weber, W.; Voice, T. Determination of partition coefficients and aqueous solubilities by reverse phase chromatography-II: evaluation of partitioning and solubility models. Water Res. 1986, 20, 1443-1450, 10.1016/0043-1354(86)90144-2

[32] Bharate Sonali, S.; Kumar, V.; Vishwakarma, R. Determining partition coefficient (logP), distribution coefficient (logD) and ionization constant (pKa) in early drug discovery. Comb. Chem. High Throughput Screening 2016, 19, 461-469, 10.2174/1386207319666160502123917

[33] Kiesgen de Richter, R.; Bonato, M.; Follet, M.; Kamenka, J. The (+)-and (-)-[2-(1,3-dithianyl)]myrtanylborane. Solid and stable monoalkylboranes for asymmetric hydroboration. J. Org. Chem. 1990, 55, 2855-2860, 10.1021/jo00296a054

[34] Dolomanov, O.; Bourhis, L.; Gildea, R.; Howard, J.; Puschmann, H. OLEX2: a complete structure solution, refinement and analysis program. J. Appl. Crystallogr 2009, 42, 339, 10.1107/S0021889808042726

[35] Sheldrick, G. SHELXT: Integrating space group determination and structure solution. Acta Crystallogr. A 2014, A70, 1437 10.1107/S2053273314085623

[36] Sheldrick, G. A short history of SHELX. Acta Crystallogr. A 2008, 64, 112-122, 10.1107/S0108767307043930

[37] Macrae, C.; Edgington, P.; McCabe, P.; Pidcock, E.; Shields, G.; Taylor, R.; Towler, M.; Streek, J. Mercury: visualization and analysis of crystal structures. J. Appl. Crystallogr. 2006, 39, 453-457, 10.1107/S002188980600731X

[38] Fischer, M.; Georges, J. Fluorescence quantum yield of rhodamine 6G in ethanol as a function of concentration using thermal lens spectrometry. Chem. Phys. Lett. 1996, 260, 115-118, 10.1016/0009-2614(96)00838-X

[39] Bogachev, M. I.; Volkov, V. Y.; Markelov, O. A.; Trizna, E. Y.; Baydamshina, D. R.; Melnikov, V.; Murtazina, R. R.; Zelenikhin, P. V.; Sharafutdinov, I. S.; Kayumov, A. R. Fast and simple tool for the quantification of biofilm-embedded cells sub-populations from fluorescent microscopic images. PLoS One 2018, 13, e0193267 10.1371/journal.pone.0193267

[40] Boichuk, S.; Galembikova, A.; Dunaev, P.; Valeeva, E.; Shagimardanova, E.; Gusev, O.; Khaiboullina, S. A novel receptor tyrosine kinase switch promotes gastrointestinal stromal tumor drug resistance. Molecules 2017, 22, 2152 10.3390/molecules22122152