

Short Note

***N*¹-(Benzo[*b*]thiophen-3-ylmethylidene)-*N*²-(2-((2-((2-(benzo[*b*]thiophen-3-ylmethylidene)amino)ethyl)amino)ethyl)amino)ethyl)ethane-1,2-diamine**

Cristina Núñez ^{1,*}, Javier Fernández-Lodeiro ², Adrián Fernández-Lodeiro ², Emília Bértolo ³, José Luis Capelo ^{1,2} and Carlos Lodeiro ^{1,2,*}

¹ REQUIMTE, Chemistry Department, Faculty of Science and Technology, University Nova of Lisbon, 2829-516 Monte de Caparica, Portugal

² BIOSCOPE Group, Physical-Chemistry Department, Faculty of Science, Ourense Campus, University of Vigo, 32004, Ourense, Spain

³ Ecology Research Group, Department of Geographical and Life Sciences, Canterbury Christ Church University, Canterbury, Kent. CT1 1QU, UK

* Authors to whom correspondence should be addressed; E-Mails: cristina.nunez@fct.unl.pt (C.N.); cle@fct.unl.pt (C.L.).

Received: 18 June 2012 / Accepted: 31 July 2012 / Published: 6 August 2012

Abstract: A novel probe **L** has been synthesized by classical Schiff-base reaction between 1-benzothiophene-3-carbaldehyde and tetraethylenepentamine as diamine. The structure of compound **L** was confirmed by melting point, elemental analysis, ESI-MS spectrometry, IR and ¹³C-NMR and ¹H-NMR spectroscopy.

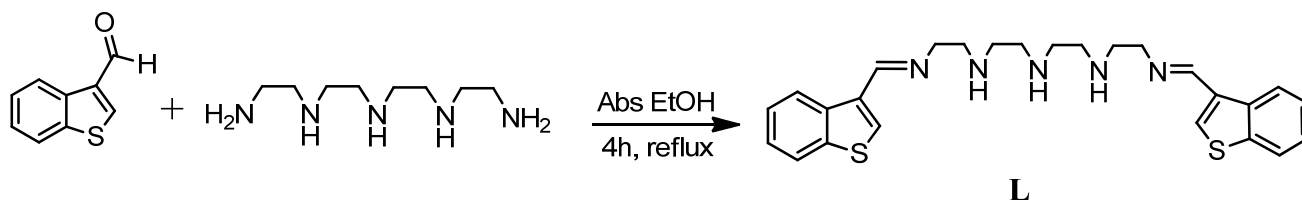
Keywords: imine compounds; amine compounds; benzothiophene units

The constant and growing interest in the development of new synthetic methods for the preparation of systems involving thiophene subunits is justified by their valuable physiological and pharmacological properties [1,2]. A large number of benzothiophene derivatives have been found to exhibit a wide variety of pharmaceutical properties such as anti-microbial [3], anti-cancer [4], and anti-HIV activity [5].

Since the last five years, our research group has been interested in the introduction of sulphur containing ligands into the skeleton of new fluorescent and colorimetric probes, and new active MALDI-TOF-MS molecules for sensing studies [6–11].

This paper describes the synthesis and characterization of a new benzothiophene di-imine probe (**L**), prepared by simple and classical Schiff-base reaction between 1-benzothiophene-3-carbaldehyde and tetraethylenepentamine (See scheme 1).

Scheme 1. Schematic representation of compound **L**.



Experimental

A solution of 1-benzothiophene-3-carbaldehyde (0.361 g, 2.108 mmol) in absolute ethanol (25 mL) was added drop wise to a refluxing solution of tetraethylenepentamine (0.199 g, 1.054 mmol) in the same solvent (35 mL). The resulting solution was gently refluxed with magnetic stirring for ca. 4 h. During that period the color changed from yellow to green. The resulting solution was concentrated under vacuum to 1/3 of its original volume. Diethyl ether was added to form a green precipitate that was filtered off and dried under vacuum. The compound isolated was characterized as chemosensor **L**.

Melting point: 123–125 °C.

Yield: 395 mg (**L**) (78%).

ESI-MS: m/z (rel. int%): 478.20 (100) [**L**+H]⁺.

¹H-NMR (CDCl₃) (**L**): δ = 8.2 (s, 2H, C–H)_{thiophene}; 8.0–7.8 (m, 8H, C–H, Ar); 7.2 (s, 2H, N=C–H); 3.8–3.2 (m, 12H, CH₂); 2.6–2.2 (m, 4H, CH₂); 1.8 (s, 3H, NH) ppm.

¹³C-NMR (CDCl₃) (**L**): δ = 160.8; 139.9; 127.9; 126.4; 124.4; 124.3; 123.2; 122.8; 119.7; 55.3; 50.2; 49.0.

IR (cm^{−1}) (**L**): 3036 (C–H, Ar), 1645 (C=N, Imine), 1598, 1493 (C=C, Ar).

Elemental analysis: Calcd for C₂₆H₃₁N₅S₂·2H₂O: C, 60.79; H, 6.87; N, 13.63. Found (**L**): C, 60.95; H, 7.20; N, 13.75.

Uv-vis (CHCl₃), [**L**] = 1.00 × 10^{−5} M, $\lambda_{\max}$ 287 and 302 nm. Non-emissive.

Acknowledgements

We are grateful to Xunta de Galicia (Spain) for projects 09CSA043383PR and 10CSA383009PR (Biomedicine) and to the Scientific Association ProteoMass for financial support. C.N. thanks the Fundação para a Ciência e a Tecnologia/FEDER (Portugal/EU) programme postdoctoral contract SFRH/BPD/65367/2009. J.F.L. thanks Xunta de Galicia (Spain) for a research contract by project

09CSA043383PR in Biomedicine. J.L.C. and C.L. thank Xunta de Galicia for the Isidro Parga Pondal Research program.

References and Notes

1. Sall, D.J.; Bailey, D.L.; Bastian, J.A.; Buben, J.A.; Chirgadze, N.Y.; Clemens-Smith, A.C.; Denney, M.L. Fisher, M.J.; Giera, D.D.; Gifford-Moore, D.S.; *et al.* Diamino Benzo[*b*]thiophene Derivatives as a Novel Class of Active Site Directed Thrombin Inhibitors. 5. Potency, Efficacy, and Pharmacokinetic Properties of Modified C-3 Side Chain Derivatives. *J. Med. Chem.* **2000**, *43*, 649–663.
2. Akay, S.; Yang, W.; Wang, J.; Lin, L.; Wang, B. Synthesis and Evaluation of Dual Wavelength Fluorescent Benzo[*b*]thiophene Boronic Acid Derivatives for Sugar Sensing. *Chem. Biol. Drug Des.* **2007**, *70*, 279–289.
3. Saravanan, G.; Alagarsamy, V.; Prakash, C.R.; Selvam, T.P.; Karthick, V.; Kumar, P.D. Synthesis and anti-microbial activities of some 3-(4-phenylthiazole-2-yl)/3-(3-carbethoxy-4,5,6,7-tetrahydrobenzothiophene-2-yl)quinazolin-4(3H)-one. *RASĀYAN J. Chem.* **2009**, *2*, 746–752.
4. Starčević, K.; Kralj, M.; Piantanida, I.; Šuman, L.; Pavelić, K.; Karminski-Zamola, G. Synthesis, photochemical synthesis, DNA binding and antitumor evaluation of novel cyano- and amidino-substituted derivatives of naphtho-furans, naphtho-thiophenes, thieno-benzofurans, benzo-dithiophenes and their acyclic precursors. *Eur. J. Med. Chem.* **2006**, *41*, 925–939.
5. Carballo, M.; Conde, M.; Tejedo, J.; Gualberto, A.; Jimenez, J.; Monteseirín, J.; Santa María, C.; Bedoya, F.J.; Hunt, S.W., III; Pintado, E.; *et al.* Macrophage inducible nitric oxide synthase gene expression is blocked by a benzothiophene derivative with anti-HIV properties. *Mol. Genet. Metab.* **2002**, *75*, 360–368.
6. Batista, R.M.F.; Oliveira, R.; Costa, S.P.G.; Lodeiro, C.; Raposo, M.M.M. Synthesis and Ion Sensing Properties of New Colorimetric and Fluorimetric Chemosensors Based on Bithienyl-Imidazo-Anthraquinone Chromophores. *Org. Lett.* **2007**, *9*, 3201–3204.
7. Batista, R.M.F.; Oliveira, R.; Costa, S.P.G.; Lodeiro, C.; Raposo, M.M.M. Synthesis and Evaluation of bipendant-armed (oligo)thiophene crown ether derivatives as new chemical sensors. *Tetrahedron Lett.* **2008**, *49*, 6575–6578.
8. Batista, R.M.F.; Oliveira, R.; Nuñez, C.; Costa, S.P.G.; Lodeiro, C.; Raposo, M.M.M. Synthesis and Evaluation of new thienyl and bithienyl-bis-indolymethanes as colorimetric sensors for anions. *J. Phys. Org. Chem.* **2009**, *22*, 362–366.
9. Oliveira, E.; Baptista, R.; Costa, S.P.G.; Raposo, M.M.M.; Lodeiro, C. Exploring the Emissive Properties of New Azacrown Compounds Bearing Aryl, Furyl and Thienyl Moieties: A Special case of Chelation Enhancement of Fluorescence upon interaction with Ca(II), Cu(II) or Ni(II). *Inorg. Chem.* **2010**, *49*, 10478–10857.
10. Oliveira, E.; Genovese, D.; Juris, R.; Zaccheroni, N.; Capelo, J.L.; Raposo, M.M.M.; Costa, S.P.G.; Prodi, L.; Lodeiro, C. Bioinspired systems for Metal-ion sensing: New emissive peptide probes based on benzo[*d*]oxazole derivatives and their gold and silica nanoparticles. *Inorg. Chem.* **2011**, *50*, 8834–8849.

11. Oliveira, E.; Nunes-Miranda, J.D.; Santos, H.M. From colorimetric chemosensors to metal nanoparticles using two new tyrosine Schiff-base ligands for Cu(II) detection. *Inorg. Chim. Acta* **2012**, *380*, 22–30.

© 2012 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 license (<http://creativecommons.org/licenses/by/3.0/>).