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Short Note

## ***N*<sup>1</sup>-Benzylidene-*N*<sup>2</sup>-(2-((2-((2-(benzylideneamino)ethyl)amino)ethyl)amino)ethyl)ethane-1,2-diamine**

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**Abstract:** A tetraethylene pentamine-diamine (**L**<sup>4</sup>), the biggest compound in the family of dibenzylated diimine-polyamines (**L**<sup>1</sup>–**L**<sup>4</sup>) has been synthesized by classical Schiff-base reaction between benzaldehyde and the diamine tetraethylenepentamine, and the structure was confirmed by elemental analysis, ESI-MS spectrometry and by IR and <sup>1</sup>H-NMR spectroscopy.

**Keywords:** imine compounds; amine compounds; polyamines; dibenzylated

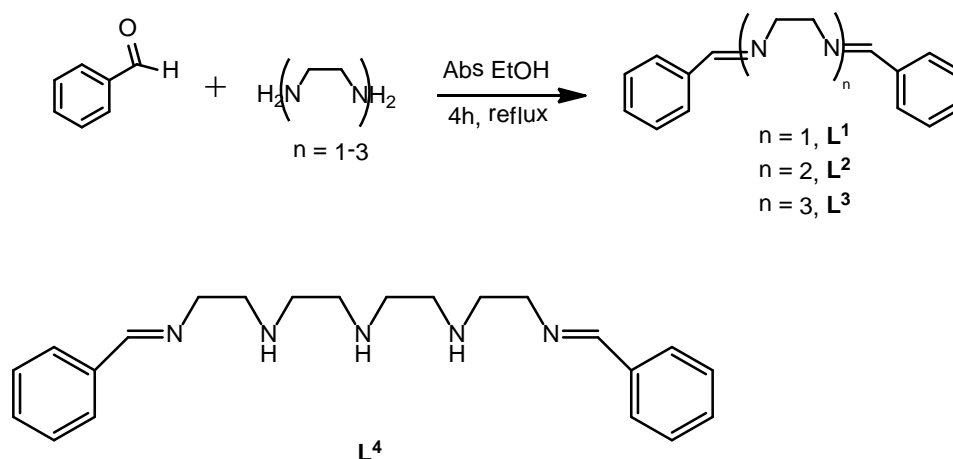
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Improved understanding of the role of polyamines in metabolism [1,2], and the differences in polyamine biology between normal cells and tumor cells [3], have increased current interest in this type of compounds in the field of drug development [4,5]. The activity of polyamines is very much dependent on their charge and the charge density they display at physiological pH [6].

During the last ten years, some of us have been involved in the studies of many different water-soluble bis-chromophoric polyamines as fluorescent chemosensors [7–10]. However, more recently studies in new active MALDI-TOF-MS matrices reveals that the introduction of imine groups into the polyamine chain increases the energy absorbed in the UV region, and consequently, the potential application as a MALDI matrix increase [11,12].

Following the method previously reported by Bernardo *et al.* for polyamine systems [13], in this paper we describe the synthesis and characterization of the tetraethylene pentamine-diamine ( $L^4$ ), derived from benzaldehyde and the diamine tetraethylenepentamine. The broader applicability of this method was demonstrated by the synthesis of a few related compounds ( $L^1$ – $L^3$ ) [14] (See scheme 1).

**Scheme 1.** Schematic representation of compounds  $L^1$ – $L^4$ .



## Experimental

A solution of benzaldehyde (0.129 g, 1.225 mmol) in absolute ethanol (20 mL) was added dropwise to a refluxing solution of tetraethylenepentamine (0.115 g, 0.612 mmol) in the same solvent (15 mL). The resulting solution was gently refluxed with magnetic stirring for 4 h. The colour changed from colourless to yellow. The solution was concentrated under vacuum to 1/3 of its volume. Diethyl ether was added to the solution and then cooled at 0 °C during 24 h. The yellow crystals formed were filtered off and dried under vacuum. At room temperature the crystals were not stable and a yellow oil was obtained.

$L^4$ :  $N^1$ -Benzylidene- $N^2$ -(2-((2-((2-(benzylideneamino)ethyl)amino)ethyl)amino)ethyl)ethane-1,2-diamine

Yield: 125 mg (56%).

ESI-MS:  $m/z$  (rel.int%): 366.26 (100) ( $[M+H]^+$ ).

$^1H$ -NMR ( $CDCl_3$ ):  $\delta$  = 8.3 (s, 2H, N=C–H); 7.5–7.7 (m, 4H, C- $H_{ar}$ ); 7.4–7.1 (m, 6H, C- $H_{ar}$ ); 3.8–3.2 (m, 4H,  $CH_2$ ); 2.9–2.1 (m, 12H,  $CH_2$ ) ppm.

IR ( $cm^{-1}$ ): 1658 (C=N, Imine), 1589, 1492 (C=C, Ar).

Elemental analysis: Calcd for  $C_{22}H_{31}N_5$ : C, 72.29; H, 8.55; N, 19.16. Found: C, 72.26; H, 7.99; N, 19.65.

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## References and Notes

1. Wallace, H.M.; Fraser, A.V.; Hughes, A. A perspective of polyamine metabolism. *Biochem J.* **2003**, *376*, 1–14.
2. Vujcic S.; Diegelman, P.; Bacchi, C.J.; Kramer, D.L.; Porter, C.W. Identification and characterization of a novel flavin-containing spermine oxidase of mammalian cell origin. *Biochem. J.* **2002**, *367*, 665–675.
3. Casero, R.A., Jr.; Marton, L.J. Targeting polyamine metabolism and function in cancer and other hyperproliferative diseases. *Nat. Rev. Drug Discov.* **2007**, *6*, 373–390.
4. Wallace, H.M.; Fraser, A.V. Polyamine analogues as anticancer drugs. *Biochem. Soc. Trans.* **2003**, *31*, 393–396.
5. Agostinelli, E.; Bachrach, U., Eds. Special issue: Polyamines and their Analogs in Cancer and other Diseases. *Amino Acids* **2007**, *33*, 175–187.
6. Sonawane, N.D.; Szoka, F.C., Jr.; Verkman, A.S. Chloride Accumulation and Swelling in Endosomes Enhances DNA Transfer by Polyamine-DNA Polyplexes. *J. Biol. Chem.* **2003**, *278*, 44826–44831.
7. Albelda, M.T.; Díaz, P.; García-España, E.; Lima, J.C.; Lodeiro, C.; de Melo, J.S.; Parola, A.J.; Pina, F.; Soriano, C. Switching from intramolecular energy transfer to intramolecular electron transfer by the action of pH and Zn(II) coordination. *Chem. Phys. Lett.* **2002**, *353*, 63–68.
8. De Melo, J.S.; Pina, J.; Pina, F.; Lodeiro, C.; Parola, A.J.; Albelda, M.T.; Clares, M.P.; García-España, E.; Soriano, C. Energetics and dynamics of naphthalene polyaminic derivatives. Influence of structural design in the balance static vs dynamic excimer formation. *J. Phys. Chem. A* **2003**, *107*, 11307–11318.
9. Alarcón, J.; Aucejo, R.; Albelda, M.T.; Alves, S.; Clares, P.; García-España, E.; Lodeiro, C.; Marchin, K.L.; Parola, A.J.; Pina, F.; *et al.* Fluorescent Type II Materials from Naphthylmethyl Polyamine Precursors. *Supramol. Chem.* **2004**, *16*, 573–580.
10. Bazzicalupi, C.; Bencini, A.; Bianchi, A.; Danesi, A.; Faggi, E.; Giorgi, C.; Lodeiro, C.; Oliveira, E.; Pina, F.; Valtancoli, B. Interaction of polyamine macrocycles with Zn(II) and ATP in aqueous solution. Binary and Ternary systems. A potentiometric, NMR and fluorescence emission studies. *Inorg. Chim. Acta* **2008**, *361*, 3410–3419.
11. Fernandez, L.; Boucher, M.; Fernández-Lodeiro, J.; Oliveira, E.; Núñez, C.; Santos, H.M.; Capelo, J.L.; Nieto-Faza, O.; Bértolo, E.; Lodeiro, C. Exploiting anionic and cationic interactions with a new emissive imine-based  $\beta$ -naphthol molecular probe. *Inorg. Chem. Commun.* **2009**, *12*, 905–912.

12. Fernández-Lodeiro, J.; Núñez, C.; Carreira, R.; Santos, H.M.; Silva-López, C.; Mejuto, J.C.; Capelo, J.L.; Lodeiro, C. Novel versatile imine-enamine chemosensor based on 6-nitro-4-oxo-4H-chromene for ion detection in solution, solid and gas-phase: Synthesis, emission, computational and MALDI-TOF-MS studies. *Tetrahedron* **2011**, *67*, 326–333.
13. Bernardo, M.A.; Gurrero, J.A.; García-España, E.; Luis, S.V.; Llinares, J.M.; Pina, F.; Ramírez, J.A.; Soriano, C. Thermodynamic, NMR and photochemical study on the acid-base behaviour of *N,N'*-dibenzylated polyamines and on their interactions with hexacyanocobaltate(III). *J. Chem. Soc. Perkin Trans 2* **1996**, 2335–2342.
14. The smaller parent compounds derived from 1,2-ethanediamine (**L**<sup>1</sup>), diethylenetriamine (**L**<sup>2</sup>), and triethylenetetramine (**L**<sup>3</sup>) were obtained by a similar methodology, using 0.038, 0.063 and 0.089 g of diamine, respectively. Compound **L**<sup>1</sup>: *N*<sup>1</sup>,*N*<sup>2</sup>-Dibenzylideneethane-1,2-diamine; Yield: 121 mg (84%); ESI-MS: *m/z* (rel. int%): 237.13 (100) ([M+H]<sup>+</sup>); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 8.1 (s, 2H, N=C–H); 7.8 (m, 4H, C-H<sub>ar</sub>); 7.2 (m, 6H, C-H<sub>ar</sub>); 3.8 (s, 4H, CH<sub>2</sub>) ppm; IR (cm<sup>-1</sup>): 1647 (C=N, Imine), 1599, 1498 (C=C, Ar); Elemental analysis: Calcd for C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>: C, 81.32; H, 6.82; N, 11.85. Found: C, 80.87; H, 7.02; N, 12.05. Compound **L**<sup>2</sup>: *N*<sup>1</sup>-Benzylidene-*N*<sup>2</sup>-(2-(benzylideneamino)ethyl)ethane-1,2-diamine; Yield: 103 mg (71%); ESI-MS: *m/z* (rel. int%): 279.17 (100) ([M+H]<sup>+</sup>); <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ = 8.2 (s, 2H, N=C–H); 7.8–7.6 (m, 4H, C-H<sub>ar</sub>); 7.4–7.2 (m, 6H, C-H<sub>ar</sub>); 3.8 (m, 4H, CH<sub>2</sub>); 2.9 (m, 4H, CH<sub>2</sub>) ppm; IR (cm<sup>-1</sup>): 1649 (C=N, Imine), 1586, 1491 (C=C, Ar); Elemental analysis: Calcd for C<sub>18</sub>H<sub>21</sub>N<sub>3</sub>: C, 77.38; H, 7.58; N, 15.04. Found: C, 77.16; H, 8.03; N, 15.34. Compound **L**<sup>3</sup>: *N*<sup>1</sup>,*N*<sup>1'</sup>-(Ethane-1,2-diyl)bis(*N*<sup>2</sup>-benzylideneethane-1,2-diamine); Yield: 132 mg (89%); ESI-MS: *m/z* (rel. int%): 323.22 (100) ([M+H]<sup>+</sup>); <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ = 8.1 (s, 2H, N=C–H); 7.7–7.5 (m, 4H, C-H<sub>ar</sub>); 7.4–7.1 (m, 6H, C-H<sub>ar</sub>); 3.7–3.4 (m, 2H, CH<sub>2</sub>); 2.9–2.1 (m, 8H, CH<sub>2</sub>) ppm; IR (cm<sup>-1</sup>): 1656 (C=N, Imine), 1576, 1499 (C=C, Ar); Elemental analysis: Calcd for C<sub>20</sub>H<sub>26</sub>N<sub>4</sub>: C, 74.50; H, 8.13; N, 17.38. Found: C, 74.78; H, 8.16; N, 17.49.

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