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Short Note

N^1-((1*H*-Indazol-5-yl)methylene)-N^2-(2-((2-((2-(((1*H*-indazol-6-yl)methylene)amino)ethyl)amino)ethyl)amino)ethyl)ethane-1,2-diamine

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Abstract: One novel molecular emissive probe **L** has been synthesized by classical Schiff-base reaction between 1H-indazole-6-carboxaldehyde and tetraethylenepentamine. The structure of compound **L** was confirmed by melting point, elemental analysis, ESI-MS spectrometry and by IR and ^{13}C-NMR and ^{1}H-NMR spectroscopy.

Keywords: imine compounds; amine compounds; indazol

Indazole ring systems have an interesting chemistry, which has been used in biology, catalysis, and medicinal chemistry [1]. Although rare in nature [2], indazoles exhibit a variety of biological activities such as HIV protease inhibition [3–5], antiarrhythmic and analgesic activities [6], antitumor activity [7,8], and antihypertensive properties [9]. Furthermore, antimicrobial and antineoplastic activities have also been shown to be associated with certain indazole derivatives [10].

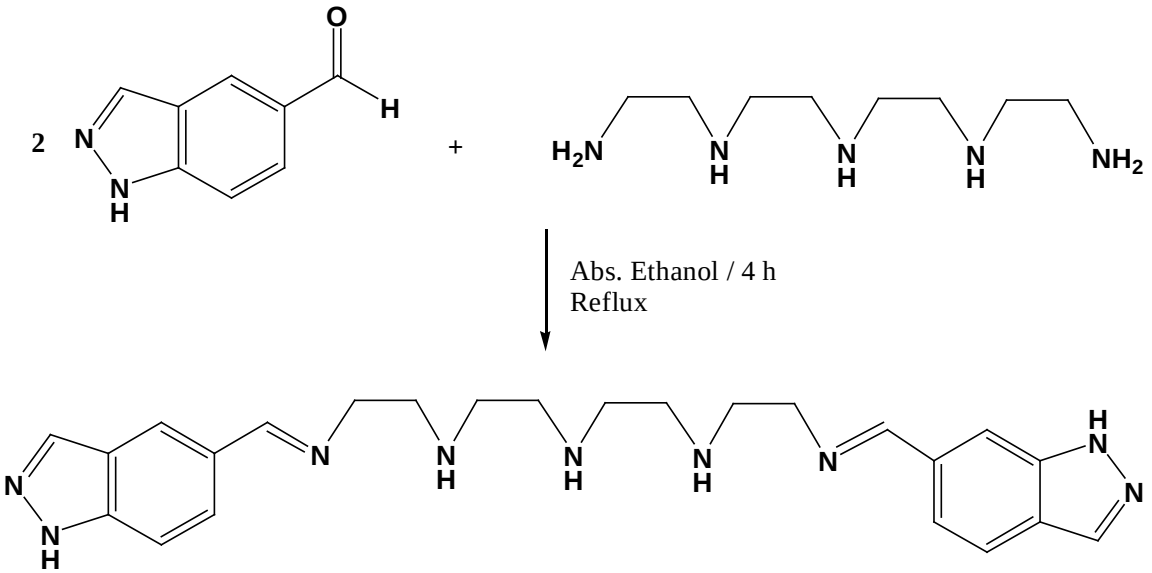
As a part of our ongoing research into the design and synthesis of novel organic molecular probes, luminescent materials and MALDI-TOF-MS matrices [11–14], here we report the synthesis and

characterization of a new Schiff-base compound **L** containing two indazole units linked by a flexible polyethylene bridged (See scheme 1).

Experimental

A solution of 1H-indazole-6-carboxaldehyde (0.254 g, 1.718 mmol) in absolute ethanol (10 mL) was added dropwise to a refluxing solution of tetraethylenepentamine (0.162 g, 0.859 mmol) in the same solvent (30 mL) (See scheme 1). The resulting solution was gently refluxed with magnetic stirring for ca. 4 h. The colour changed from yellow to brown. After that time, the mixture was allowed to cool to room temperature and a brown powder precipitate was formed; this was then filtered off, washed with cold absolute ethanol and cold diethyl ether and dried under vacuum. The resulting compound was characterized as **L** follow purification by column chromatography.

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



Melting point: 163–165 °C.

Yield: 382 mg (**L**) (93%).

ESI-MS: *m/z* (rel. int%): 446.27 (100) ([**L**+H]$^+$.

^{1}H-NMR ($CDCl_3$) (**L**): δ = 12.1 (s, 2H, N–H); 8.4 (s, 2H, N=C–H); 8.2–7.0 (m, 6H, C-H_{ar}); 3.9–2.1 (m, 16H, CH_2); 1.5 (s, 3H, NH) ppm.

^{13}C-NMR ($CDCl_3$) (**L**): δ = 160.5; 150.3; 147.2; 133.6; 131.2; 127.9; 126.1; 125.0; 124.2; 119.7; 112.3; 110.4; 56.2; 50.6; 49.8.

IR (cm^{-1}) (**L**): 3051 (C–H, Ar), 1638 (C=N, Imine), 1618, 1593, 1562 and 1509 (C=C, Ar).

Elemental analysis: Calcd for $C_{24}H_{37}N_9O_3$: C, 57.70; H, 7.45; N, 25.25. Found (**L**): C, 58.00; H, 7.15; N, 25.00.

Uv-vis ($CHCl_3$), [**L**] = 1.00×10^{-5} M, λ_{max} 275 and 324 nm.

Fluorescence Emission ($CHCl_3$); [**L**] = 1.00×10^{-5}): λ_{max} 427 nm.

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References and Notes

1. Sather, A.C.; Berryman, O.B.; Rebek, J., Jr. Synthesis of Fused Indazole Ring Systems and Application to Nigeglanine Hydrobromide. *Org. Lett.* **2012**, *14*, 1600–1603.
2. Ali, Z.; Ferreira, D.; Carvalho, P.; Avery, M.A.; Khan, I.A. Nigellidine-4-*O*-sulfite, the First Sulfated Indazole-Type Alkaloid from the Seeds of *Nigella sativa*. *J. Nat. Prod.* **2008**, *71*, 1111–1112.
3. Han, W.; Pelletier, J.C.; Hodge, C.N. Tricyclic ureas: A new class of HIV-1 protease inhibitor. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3615–3620.
4. Patel, M.; Rodgers, J.D.; McHugh, R.J., Jr.; Johnson, B.L.; Cordova, B.C.; Klaba, R.M.; Bacheler, L.T.; Erickson-Viitanen, S.; Ko, S.S. Unsymmetrical cyclic ureas as HIV-1 protease inhibitors: Novel biaryl indazoles as P2/P2′ substituents. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 3217–3220.
5. Sun, J.-H.; Teleha, C.A.; Yan, J.-S.; Rodgers, J.D.; Nugiel, D.A. Efficient Synthesis of 5-(Bromomethyl)- and 5-(Aminomethyl)-1-THP-Indazole. *J. Org. Chem.* **1997**, *62*, 5627–5629.
6. Mosti, L.; Menozzi, G.; Fossa, P.; Filippelli, W.; Gessi, S.; Rinaldi, B.; Falcone, G. Synthesis and preliminary biological evaluation of novel N-substituted 1-amino-3-[1-methyl(phenyl)-1H-indazol-4-yloxy]-propan-2-ols interesting as potential antiarrhythmic, local anaesthetic and analgesic agents. *Arzneimittelforschung* **2000**, *50*, 963–972.
7. Jakupec, M.A.; Reisner, E.; Eichinger, A.; Pongratz, M.; Arion, V.B.; Galanski, M; Hartinger, C.G.; Keppler, B.K. Redox-Active Antineoplastic Ruthenium Complexes with Indazole: Correlation of in Vitro Potency and Reduction Potential. *J. Med. Chem.* **2005**, *48*, 2831–2837.
8. Showalter, H.D.H.; Angelo, M.M.; Berman, E.M.; Kanter, G.D.; Ortwine, D.F.; Ross-Kesten, S.G.; Sercel, A.D.; Turner, W.R.; Werbel, L.M.; Worth, D.F.; *et al*. Benzothiopyranoindazoles, a New Class of Chromophore Modified Anthracenedione Anticancer Agents. Synthesis and Activity against Murine Leukemias. *J. Med. Chem.* **1988**, *31*, 1527–1539.
9. Goodman, K.B.; Cui, H.; Dowdell, S.E.; Gaitanopoulos, D.E.; Ivy, R.L.; Sehon, C.A.; Stavenger, R.A.; Wang, G.Z.; Viet, A.Q.; Xu, W.; *et al*. Development of Dihydropyridone Indazole Amides as Selective Rho-Kinase Inhibitors. *J. Med. Chem.* **2007**, *50*, 6–9.

10. Raffa, D.; Daidone, G.; Maggio, B.; Schillaci, D.; Plescia, F. Synthesis and Antiproliferative Activity of Novel 3-(Indazol-3-yl)-quinazolin-4(3*H*)-one and 3-(Indazol-3-yl)-benzotriazin-4(3*H*)-one Derivatives. *Arch. Pharm. Pharm. Med. Chem.* **1999**, *332*, 317–320.
11. Lodeiro, C.; Pina, F. Luminescent and chromogenic molecular probes based on polyamines and related compounds. *Coord. Chem. Rev*. **2009**, *253*, 1353–1385.
12. Lodeiro, C.; Capelo, J.L.; Mejuto, J.C.; Oliveira, E.; Santos, H.M.; Pedras, B.; Nuñez, C. Light and colour as analytical detection tools: A journey into the periodic table using polyamines to bio-inspired systems as chemosensors. *Chem. Soc. Rev.* **2010**, *39*, 2948–2976.
13. Bastista, R.M.F.; Oliveira, E.; Costa, S.P.G.; Lodeiro, C.; Raposo, M.M.M. Imidazo-benzo-15-crwon-5 ethers bearing arylthienyl and bithienyl moieitis as novel fluorescent chemosensor for Pd(II) and Cu(II). *Tetrahedron* **2011**, *67*, 7106–7113.
14. Fernández-Lodeiro, J.; Nuñez, C.; Carreira, R.; Santos, H.M.; López, C.S.; 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.