molbank

MDPI

Communication

Synthesis and Characterization of 2-(((2,7-Dihydroxynaphthalen-1-yl)methylene)amino)-3′,6′-bis(ethylamino)-2′,7′-dimethylspiro[isoindoline-1,9′-xanthen]-3-one and Colorimetric Detection of Uranium in Water

Rahisa Mohammed [1], Peace Ogadi [1], Dennis M. Seth Jr. [2], Amrutaa Vibho [1], Sarah K. Gallant [1*], and Rory Waterman [2]

[1] Department of Chemistry and Biochemistry, Norwich University, VT, USA
[2] Department of Chemistry, University of Vermont, VT, USA
* Correspondence: sgallant@norwich.edu

Abstract: 2-(((2,7-Dihydroxynaphthalen-1-yl)methylene)amino)-3′,6′-bis(ethylamino)-2′,7′-dimethylspiro[isoindoline-1,9′-xanthen]-3-one was synthesized using Rhodamine 6G hydrazide (prepared by literature methods) and commercially available 2,7-dihydroxynaphthalene-1-carbaldehyde via imine condensation. Structural characterization was performed using FT-IR, ^{1}H-NMR, ^{13}C-NMR, X-Ray, and HRMS. This Schiff base shows promise as a ligand for colorimetric analysis of uranium in water.

Keywords: Schiff base; ligand; colorimetric analysis

1. Introduction

Schiff bases are a class of compounds derived from the reaction of primary amines with carbonyl compounds, resulting in the formation of an imine (C=N) [1]. Structurally these compounds are well suited for binding transition metals [2,3,4], and Schiff bases have commonly been used as fluorescent or colorimetric probes for metal ions [5,6]. These molecules are highly tunable due to their modular synthesis, and varying the structure has been shown to result in high selectivity for a particular metal ion in solution, even in the presence of competing metal ions [6].

Industrially, Schiff bases have been used as catalysts, dyes, or stabilizers [7]. These compounds have also been thoroughly investigated for their high levels of biological activity as metal complexes [8] or as small molecule candidates for anticancer activity [9] as well antiviral, antibacterial, and anti-inflammatory properties, among others [7].

The following work demonstrates the synthesis and characterization of 2-(((2,7-dihydroxynaphthalen-1-yl)methylene)amino)-3′,6′-bis(ethylamino)-2′,7′-dimethylspiro[isoindoline-1,9′-xanthen]-3-one (**PROM1**), a Schiff base synthesized from Rhodamine 6G hydrazide and 2,7-dihydroxynaphthalene-1-carbaldehyde. A related Schiff base was previously reported and shown to have high uranium binding affinity [10]. **PROM1** was also tested as a ligand for colorimetric sensing of uranium in water.

2. Results and Discussion

2.1 Synthesis of 2-(((2,7-dihydroxynaphthalen-1-yl)methylene)amino)-3′,6′-bis(ethylamino)-2′,7′-dimethylspiro[isoindoline-1,9′-xanthen]-3-one (**PROM1**)

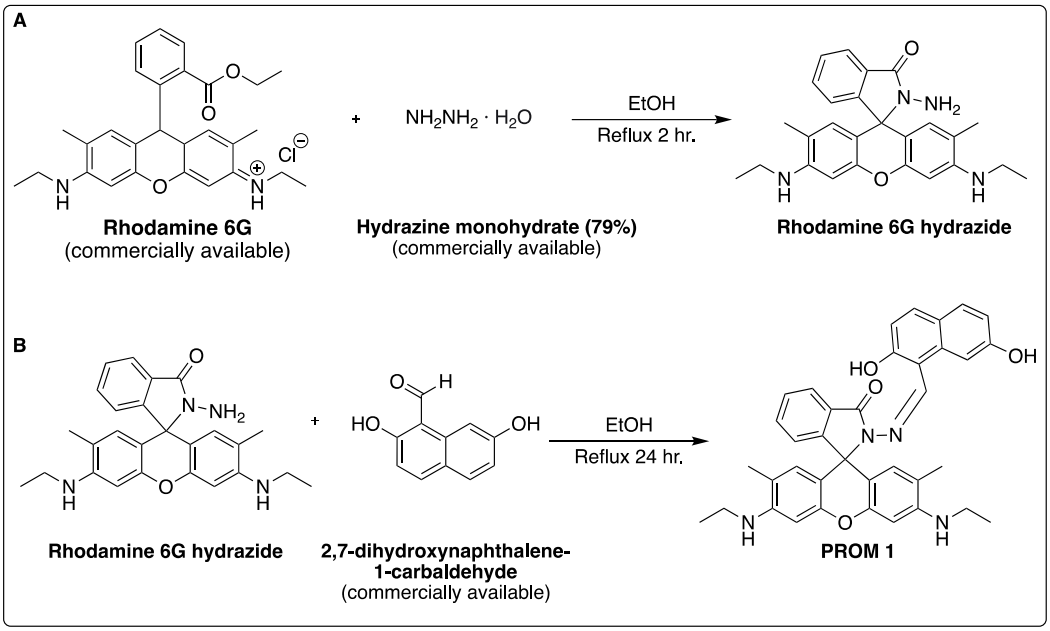
Schiff base **PROM1** was synthesized in two steps. First, rhodamine 6G hydrazide was prepared using literature methods (Scheme 1a)[11]. This starting material was then used

Citation: To be added by editorial staff during production.

Academic Editor: Firstname Lastname

Received: date
Revised: date
Accepted: date
Published: date

for imine condensation with commercially available 2,7-dihydroxynaphthalene-1-carbaldehyde via overnight reflux (Scheme 1b).



Scheme 1. A) Synthesis of Rhodamine 6G hydrazide via literature procedure [11]. B) Synthesis of **PROM1** ligand.

PROM1 was recrystallized by slow evaporation in a mixture of acetonitrile and ethanol. The crystalline product was analyzed by X-Ray, FT-IR, high-resolution ESI-MS, ^{1}H- and ^{13}C-NMR (for spectra see Supplementary Materials, Figures S1-S6). Structural determination of **PROM1** was performed via X-ray crystallography (Figure 1), and the structure was confirmed by NMR spectroscopy.

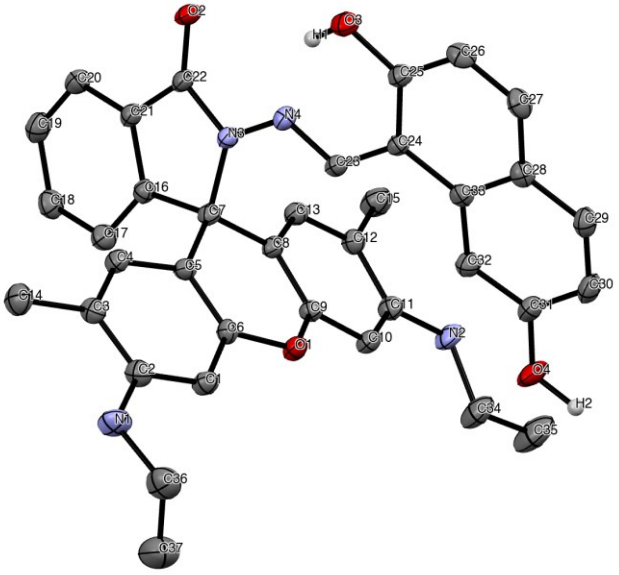


Figure 1. Molecular structure of **PROM1**•2 MeCN with thermal ellipsoids drawn at a 30% probability level. The solvent molecules are not shown, and H atoms are omitted except on heteroatoms for clarity.

2.2 Colorimetric Detection of Uranium

Uranium is a chemically and radiologically toxic element that occurs naturally in groundwater, and may have increased concentrations due to mining operations, processing for nuclear power, or improper nuclear waste management [12]. A simple colorimetric test for the presence of uranium in drinking water may prevent accidental exposure to uranium, which can result in kidney disease, kidney failure, or cancer [13].

A stock solution of **PROM1** was dissolved in dimethylsulfoxide. When mixed with aqueous solutions of uranyl nitrate, a color change from yellow to pink could be observed (Figure 2).

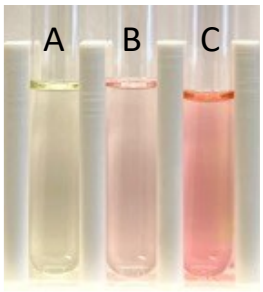


Figure 2. A) A stock solution of **PROM1** in DMSO. B) **PROM1** and 500 μg/L uranyl nitrate in 50/50 DMSO and water. C) **PROM1** and 5,000 μg/L uranyl nitrate in 50/50 DMSO and water.

3. Materials and Methods

3.1 General

All starting materials were purchased from commercial suppliers. Rhodamine 6G and 2,7-dihydroxynaphthalene-1-carbaldehyde were purchased from Sigma Aldrich, 80% hydrazine from TCI (VWR), and uranyl nitrate hexahydrate from Fisher Scientific. Solvents were reagent/ACS grade and were purchased from VWR. Rhodamine 6G hydrazide was synthesized as described previously in the literature [11].

The IR spectrum was recorded on a Perkin Elmer Spectrum 100 FT-IR, UV-Vis spectra were recorded on a Shimadzu UV-2600i, mass spectrometry was run by direct infusion in pos ESI on an Agilent 6530 QToF HRMS, NMR spectra were collected on a Bruker AXR 500 MHz spectrometer in dimethylsulfoxide-d_6 solution with reference to residual solvent signals (DMSO-d_6, δ = 2.50 ppm for ^{1}H and 39.52 ppm for ^{13}C). X-ray diffraction data was collected on a Bruker APEX 2 CCD platform diffractometer [Mo Kα (λ = 0.71073 Å)].

*3.2 2-(((2,7-dihydroxynaphthalen-1-yl)methylene)amino)-3′,6′-bis(ethylamino)-2′,7′-dimethylspiro[isoindoline-1,9′-xanthen]-3-one (**PROM1**)*

To Rhodamine 6G hydrazide (0.1915g, 0.45 mmol) was added a solution of ethanol (15ml), and acetic acid (5-6 drops). The mixture was stirred to dissolve, then 2,7-dihydroxynaphthalene-1-carbaldehyde (0.0837g, 0.44 mmol) was added. The resulting solution was stirred for 24 hr under reflux at 72 °C. The yellow solid product was separated by hot vacuum filtration (0.1839, 68.8%). A portion of the product was redissolved in warm acetonitrile, layered with ethanol and recrystallized by slow evaporation at 5 °C. The yellow crystalline product was used directly for X-Ray, ^{1}H and ^{13}C NMR, and HRMS. HRMS *m*/*z* calcd. for $C_{37}H_{34}N_4O_4$: 598.26. Found($M+H^+$): 599.2641.

^{1}H-NMR (DMSO-d_6): 9.57 (s, 1H, imine-H), 8.00 (d, J= 7.3, 1H, Ar-H), 7.73 (d, J = 8.9, 1H, Ar-H), 7.70-7.63 (m, 3H, Ar-H), 7.13-7.11 (overlapping m, 2H, Ar-H), 6.95 (dd, J = 8.70, 1.96, 1H, Ar-H), 6.82 (d, J = 8.9, 1H, Ar-H), 6.40 (s, 2H, Ar-H), 6.27 (s, 2H, Ar-H), 3.46 (residual water), 3.16 (q, J = 6.58, 4H, N-Et CH_2), 2.54 (DMSO), 2.10 (s, MeCN), 1.87 (s, 6H, Ar-CH_3), 1.22 (t, J = 7.09, 6H N-Et CH_3), 1.09 (t, J = 7, EtOH). ^{13}C-NMR (DMSO-d_6): 163.5 (s), 158.5 (s), 157.4 (s), 151.4 (s), 151.2 (s), 148.1 (s), 147.2 (s), 134.1 (s), 133.7 (s), 133.1 (s), 130.8 (s), 129.0 (s), 128.6 (s), 127.0 (s), 124.0 (s), 123.1 (s), 122.2 (s), 118.7 (s), 118.1 (s, MeCN), 115.6 (s), 115.2 (s), 107.0 (s), 103.9 (s), 102.7 (s), 95.7 (s), 65.6 (s), 56.1 (s, EtOH), 39.5 (q, DMSO), 37.5 (s), 18.6 (s, EtOH), 17.0 (s), 14.1 (s), 1.22 (s, MeCN).

3.3 X-Ray Data

X-ray diffraction data were collected on a Bruker APEX 2 CCD platform diffractometer (Mo Kα (λ = 0.71073 Å)) at 150(2) K. A suitable yellow crystal, grown from acetonitrile and ethanol, was mounted on a MiTiGen micromount with Paratone-N cryoprotectant oil. The structure was solved by direct methods using SHELXT and refined by full-matrix least-squares methods against F^2 by SHELXL-2018/3 [14, 15]. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined with isotropic displacement parameters. H1 and H2 were refined freely. Hydrogen atoms on carbon were included in calculated positions and were refined using a riding model.

Crystallographic data for the structure reported here have been deposited with the Cambridge Crystallographic Data Centre [16]. CCDC 2287758 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures. The final CIF file was generated using FinalCif [17].

Crystal Data for $C_{41}H_{40}N_6O_4$ (M = 680.79g/mol): triclinic, space group P–1 (no. 2), a = 11.37(3) Å, b = 11.51(3) Å, c = 14.38(3) Å, α = 80.06(3) °, β = 74.82(3)°, γ = 85.75(3) °, V = 1789(7) Å^3, Z = 2, T = 150(2) K, μ(MoKα) = 0.083 mm^{-1}, D_{calc} = 1.264 g/cm^3, 14714 reflections measured (3.59° $\leqslant 2\Theta \leqslant$ 47.48°), 5320 unique (Rint = 0. 0799, Rsigma = 0.0952) which were used in all calculations. The final R1 was 0.0450 (I > 2σ(I)) and wR2 was 0.1066 (all data).

3.4 Colorimetric Analysis of Uranium Binding

Stock solutions of uranyl nitrate in water were prepared by dissolving the appropriate amounts of solid uranyl nitrate hexahydrate in DI water. The **PROM1** stock solution was prepared by dissolving 0.0200 g (0.033 mmol) in 100 mL of DMSO. Equal amounts of the ligand stock solution (in DMSO) and uranyl nitrate hexahydrate solution (in water) were then mixed resulting in the yellow to pink color change upon uranium binding (Figure 2).

4. Conclusions

Novel Schiff base 2-(((2,7-dihydroxynaphthalen-1-yl)methylene)amino)-3′,6′-bis(ethylamino)-2′,7′-dimethylspiro[isoindoline-1,9′-xanthen]-3-one (**PROM1**) was synthesized from Rhodamine 6G

hydrazide and 2,7-dihydroxynaphthalene-1-carbaldehyde. **PROM1** was shown to bind uranium in water and is a plausible ligand for colorimetric analysis of uranium in drinking water.

Supplementary Materials: The following supporting information can be downloaded online. The supplementary materials contain the NMR spectra of **PROM1** (Figures S1-S4), IR spectrum (Figure S5) and HRMS (Figure S6).

Author Contributions: R. M. and P. O. synthesized and recrystallized the target compound; A. V. performed colorimetric experiments; D. S. carried out crystallographic experiments and NMR characterization; R.W. assisted with reviewing and editing as well as compound analysis; S.G. conceptualized the project, acquired funding, analyzed data, and wrote the original draft. All authors have read and agreed to the published version of the manuscript.

Funding: This research was supported by an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under grant number P20GM103449. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of NIGMS or NIH. Additional support was provided by U. S. National Science Foundation through CHE-2101766 and CHE-1039436.

Data Availability Statement: The authors confirm that the data supporting the findings of this study are available within the article [and/or] its Supplemental Materials.

Acknowledgments: S.G., R. M., P.O., and A.V. would like to thank the Norwich University Department of Chemistry and Biochemistry, the Norwich University Office of Academic Research, and the Vermont Biomedical Research Network for their support. The authors would also like to thank Bruce O'Rourke for his assistance with HRMS.

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

References

1. Raczuk, E.; Dmochowska, B.; Samaszko-Fiertek, J.; Madaj, J. Different Schiff Bases—Structure, Importance and Classification. *Molecules* **2022**, *27*, 787. DOI: https://doi.org/10.3390/molecules27030787.

2. Hunter, L.; Marriott, J.A. Co-ordinated copper and nickel compounds of salicylidene derivatives. *J. Chem. Soc.***1937**, *422*, 2000–2003. DOI: https://doi.org/10.1039/JR9370002000.

3 . Sacconi, L.; Ciampolini, M.; Maggio, F.; Cavasini, F.P. Studies in Coordination Chemistry. IX.1Investigation of the Stereochemistry of Some Complex Compounds of Cobalt(II) with N-Substituted Salicylaldimines. *J. Am. Chem. Soc.* **1962**, *84*, 3246–3248. DOI: https://doi.org/10.1021/ja00876a005.

4 . Holm, R.H.; Swaminathan, K. Studies on Nickel(II) Complexes. III. Bis-(N-arylsalicylaldimine) Complexes. *Inorg. Chem.* **1962**, *1*, 599–607. DOI: https://doi.org/10.1021/ic50003a030.

5. Wang, Y.; Hao, X.; Liang, L.; Gao, L.; Ren, X.; Wu, Y.; Zhao, H. A coumarin-containg Schiff base fluorescent probe with AIE effect for the copper(II) ion. *RSC Adv.*, **2020**, *10*, 6109. DOI: https://doi.org/10.1039/C9RA10632D.

6. Khan, S.; Chen, X.; Almahri, A.; Allehyani, E. S.; Alhumaydhi, F. A.; Ibrahim, M. M.; Ali, S. Recent developments in fluorescent and colorimetric chemosensors based on schiff bases for metallic cations detection: A review. *Journal of Environmental Chemical Engineering* **2021**, *9* (6), 106381. DOI: https://doi.org/10.1016/j.jece.2021.106381.

7. Uddin, M. N.; Ahmed, S. S.; Alam, S. M. R. REVIEW: Biomedical applications of Schiff base metal complexes. *Journal of Coordination Chemistry* **2020**, *73* (23), 3109-3149. DOI: 10.1080/00958972.2020.1854745.

8. a) Chaudhary, N.K.; Mishra, P. Metal complexes of a novel Schiff base based on penicillin: Characterization, molecular modeling, and antibacterial activity study. *Bioinorg. Chem. Appl.* **2017**, *2017*, 6927675. DOI: https://doi.org/10.1155/2017/6927675. b) Chaudhary, N.K.; Mishra, P. Bioactivity of some divalent M(II) complexes of penicillin based Schiff base ligand: Synthesis, spectroscopic characterization, and thermal study. *J. Saudi Chem. Soc.* **2018**, *22*, 601–613. DOI: https://doi.org/10.1016/j.jscs.2017.10.003. c) Sridhar, G.; Bilal, M.; Easwaramoorthy, D.; Rani, K.; Kumar, S.; Manohar, C.S. Synthesis, Characterization and Antimicrobial Activities of Copper, Nickel, Cobalt, Chromium Complexes Derived from (Z)-4-Fluoro-N-(2,7-dimethylhept-6-enylidene) benzenamine. *J. Braz. Chem. Soc.* **2017**, *28*, 756–767. DOI: http://dx.doi.org/10.21577/0103-5053.20160224.

9. Uddin, N.; Rashid, F.; Ali, S.; Tirmizi, S. A.; Ahmad, I.; Zaib, S.; Zubair, M.; Diaconescu, P. L.; Tahir, M. N.; Iqbal, J.; et al. Synthesis, characterization, and anticancer activity of Schiff bases. *Journal of Biomolecular Structure and Dynamics* **2020**, *38* (11), 3246-3259. DOI: 10.1080/07391102.2019.1654924.

10. Halali, V. V.; Balakrishna, R. G. An expeditious method for the ultra-level chemosensing of uranyl ions. *Anal. Methods* **2020**, *12* (8), 1070-1076. DOI: 10.1039/c9ay02715g.

11. Zhang, Z.; Zheng, Y.; Hang, W.; Yan, X.; Zhao, Y. Sensitive and selective off-on rhodamine hydrazide fluorescent chemosensor for hypochlorous acid detection and bioimaging. *Talanta* **2011**, *85*, 779-786. DOI: 10.1016/j.talanta.2011.04.078.

12. Jalbani, N.; Soylak, M. Spectrophotometric determination of uranium using chromotrope 2R complexes. *J. Radioanal. Nucl. Chem.* **2014**, *301* (1), 263-268. DOI: 10.1007/s10967-014-3132-z.

13. Srivastava, P. K. Spectrophotometric analysis of underground well water uranium of abandoned coal mines. *IOSR J. Environ. Sci., Toxicol. Food Technol.* **2016**, *10* (11-1), 101-105. DOI: 10.9790/2402-101101101105.

14. G. M. Sheldrick, *Acta Cryst.* **2015**, *A71*, 3–8, doi:10.1107/S2053273314026370.

15. G. M. Sheldrick, *Acta Cryst.* **2015**, *C71*, 3–8, doi:10.1107/S2053229614024218.

16. C. R. Groom, I. J. Bruno, M. P. Lightfoot, S. C. Ward, *Acta Cryst.* **2016**, *B72*, 171–179, doi:10.1107/S2052520616003954.

17. D. Kratzert, *FinalCif*, *V123*, https://dkratzert.de/finalcif.html.