

Synthesis and characterization of bis-azo 1,2,4,5-tetrazine dyestuff

Tawfik A. Khattab* and Mohamed Rehan

Textile Industries Research Division, National Research Centre, Cairo 12622, Egypt

THE synthesis and characterization of symmetrical 3,6-Bis(2-(4-(dodecyloxy)phenyl)-1-(4-(phenyl)diazene)-1,2,4,5-tetrazine were reported. Our new symmetrical bis-azo tetrazine was obtained via addition reaction of 4-(2-(4-decyloxyphenyl)diazenyl)benzotrile with hydrazine hydrate and then subjected to oxidation process. The molecular structure was verified by different analytical techniques including fourier-transform infrared spectroscopy (FT-IR), elemental analysis and nuclear magnetic resonance (¹H- and ¹³C-NMR) spectral measurements.

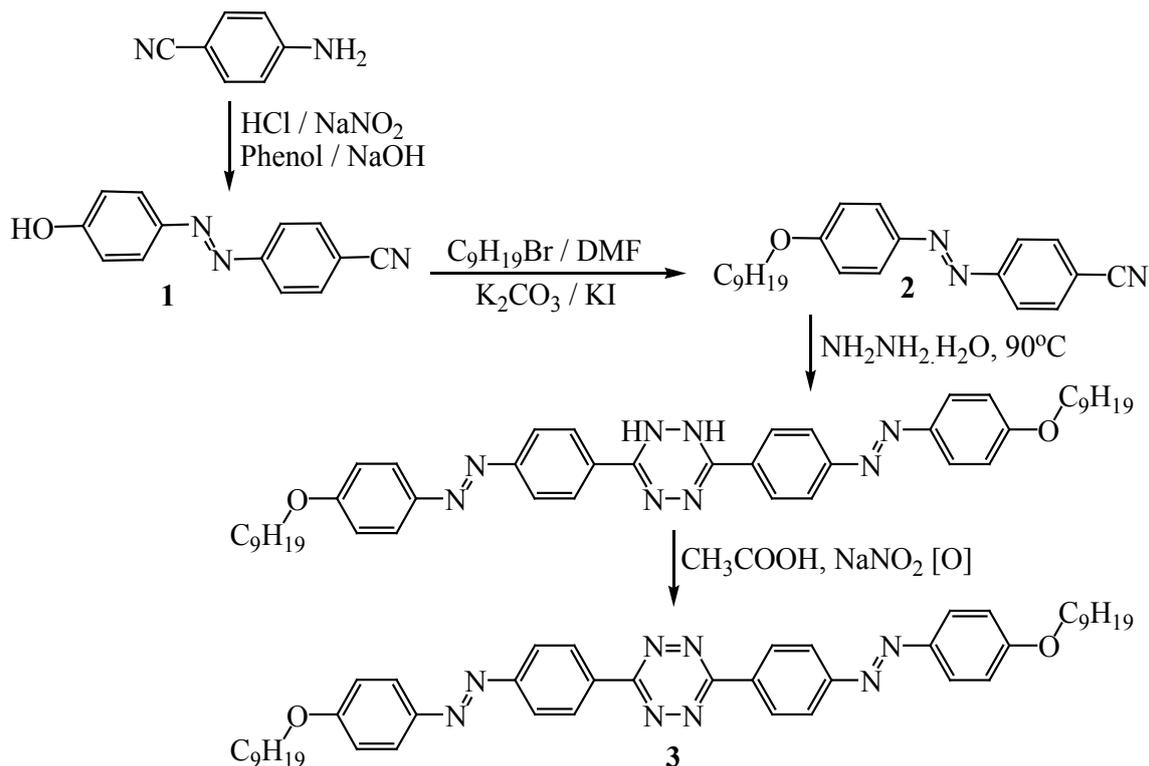
As a result of the large range of applications of tetrazine-based products, the inclusion of a heterocyclic tetrazine moiety in molecular structures of different compounds affords such materials new significant properties [1, 2]. Symmetrical tetrazine-based materials are a famous group of aromatic heterocyclics that have been applied in a diversity of research areas, such as anti-tumors, metallo-supramolecular self-assembly, insecticides, electrochemical materials, fluorescent products, electroactive materials, bio-orthogonal label and cell sensing [3-9]. Tetrazines can be considered as one of the highest electron deficient aromatic compounds. They are able to introduce high electron-affinity and charge-transfer as conjugated chemical materials. Tetrazines display brilliant shades and their emission properties can be selectively quenched by electron rich compounds [10-12]. Tetrazines have been also interested as sensors in the molecular detection of ecological contaminants, as anion binders and in metallic coordination. They are readily able to interact in inverse-demand Diels-Alder. These high nitrogen-containing energetic 1,2,4,5-tetrazines are well known for their application as propellants, explosives and pyrotechnic ingredients [13-16]. In this research study, we depict the synthetic approach of bis-azo symmetrical tetrazine.

As shown in Scheme 1 and according to literature procedures [12, 17-19], the 4-(2-(4-hydroxyphenyl)diazenyl)benzotrile **1** was prepared starting from 4-cyanoaniline which afforded the diazonium salt followed by azo-coupling with phenol. The compound 4-(2-(4-nonyloxyphenyl)diazenyl)benzotrile **2** was prepared from a mixture of compound **1**, anhydrous potassium carbonate, bit of potassium iodide, and 1-bromononane in dry DMF at 60°C to afford an orange powder with a relatively good yield. Our target compound 3,6-bis(2-(4-(nonyloxy)phenyl)-1-(4-(phenyl)diazene)-1,2,4,5-tetrazine **3** was synthesized from **2** via addition interaction with hydrazine hydrate to give the dihydrotetrazine intermediate, which was then subjected to oxidation employing sodium nitrite to give the bis-azo 1,2,3,4-tetrazine product **3** in a moderate yield.

* Corresponding Author: Tawfik A. Khattab; Email: ta.khattab@nrc.sci.eg

DOI: 10.21608/JTCPS.2018.5033.1003

©2018 National Information and Documentation Centre (NIDOC)



Scheme 1. Synthetic path for new bis-azo sym-tetrazine chromophore 3.

From the $^1\text{H-NMR}$ spectrum of the tetrazine compound **3**, the three peaks at 8.16, 7.87, 7.13 ppm were attributed to the four phenyl azo moieties, while the $^{13}\text{C-NMR}$ displayed nine signals in the aromatic area and nine signals for the aliphatic moieties. Our bis-azo *sym*-tetrazine dye can be applied as disperse dyestuff for hydrophobic fibers, such as polyester since it can be acknowledged as a non-ionic small-size molecular structure with a very low solubility in water. In conclusion, a new bis-azo *sym*-tetrazine was effectively prepared and verified according to FT-IR, elemental analysis, and $^1\text{H-}$ and $^{13}\text{C-NMR}$ spectroscopic methods.

Experimental details

Materials and Methods

Melting points were measured on Stuart SMP30 and were recorded uncorrected in degree Celsius ($^{\circ}\text{C}$). Fourier-transform infrared (FT-IR) spectra were determined by a JASCO FT/IR-4700 spectrophotometer with a spectral resolution of 4 cm^{-1} and in the wavenumber range of $400\text{--}4000\text{ cm}^{-1}$. Elemental analyses (C, H, N) was made

using PerkinElmer 2400 analyzer (PerkinElmer, Norwalk, CT, United States). NMR spectra were reported by a BRUKER AVANCE 400 spectrometer at 400 MHz; chemical shifts were recorded in ppm relative to tetramethylsilane internal standard.

Solvents employed in this research study were obtained from Fluka and Aldrich for both of the preparation processes and spectroscopic measurements (spectroscopic grade). Compounds **1** and **2** were synthesized according to literature procedure [17, 18] starting from 4-cyanoaniline which is a commercial material from Sigma-Aldrich. All reactions were followed by thin layer chromatography (TLC) employing Merck aluminum plates pre-coated with silica gel PF254; $20\times 20\text{ cm}$, 0.25 mm , and monitored visually under UV lamp (254 or 365nm).

Synthetic approaches:

Synthesis of 4-(2-(4-hydroxyphenyl)diazenyl) benzonitrile (1)

Prepared from 4-cyanoaniline (10 mmol) was dissolved in HCl (37%; 15 mL), cooled to $0\text{--}5^{\circ}\text{C}$ in an ice-bath with stirring and subjected to diazotization by slow addition of a solution of sodium nitrite (10 mmol) in distilled water

(5 mL). Phenol (10 mmol) was then dissolved in 10 wt% of NaOH solution (10 mL) and cooled to 0-5°C and the cold diazonium salt solution was added dropwise. The mixture was acidified using aqueous HCl to afford an orange precipitate which was filtered off, washed with distilled water, air dried and recrystallized from ethanol to get an orange powder (yield 76%). m.p.>300°C. ¹H-NMR (400 MHz, DMSO-d₆) ppm: δ 10.57 (s, 1H, ArOH), 8.03 (d, 2H), 7.92 (d, 2H), 7.85 (d, 2H), 6.96 (d, 2H).

Synthesis of 4-(2-(4-nonyloxyphenyl)diazanyl)benzonitrile (2)

A mixture of 4-(4'-hydroxyphenylazo) benzonitrile (10 mmol), anhydrous potassium carbonate (20 mmol), bit of potassium iodide, and 1-bromononane (10 mmol) was stirred under nitrogen in dry DMF (15 mL) at 60°C for 8 hours. The mixture was then added to cold distilled water to afford solid precipitate which was isolated by filtration and washed with distilled water then hexane. An orange powder was obtained (yield 76%). m.p. 106-108°C. ¹H-NMR (400 MHz, CDCl₃) ppm: δ 7.96 (dd, 4H), 7.81 (d, 2H), 7.04 (d, 2H), 4.05 (t, 2H), 1.81 (q, 2H), 1.47 (m, 2H), 1.32 (m, 8H), 1.28 (t, 2H), 0.92 (t, 3H).

Synthesis of 3,6-Bis(2-(4-(nonyloxy)phenyl)-1-(4-phenyl)diazene)-1,2,4,5-tetrazine (3)

A mixture of compound **2** (10 mmol) and excess of hydrazine hydrate (8 mL) was heated at 90°C in an oil bath for 9 hours. After cooling to ambient temperature, the produced precipitate was filtered off, washed with hexane and recrystallized from ethanol to give a red solid (yield 56%). The produced compound (5 mmol) was stirred in glacial CH₃COOH (10 mL) and then a 10 mL solution of NaNO₂ (5 equiv.) was added slowly over 8 minutes with stirring. The mixture was stirred for an extra 20 minutes; the residual was isolated by filtration, washed with hexane, and finally air-dried to give a red powder (yield 68%). m.p.>300°C. ¹H NMR (400 MHz, DMSO-d₆) ppm: δ 8.16 (d, 4H), 7.87 (dd, 8H), 7.13 (d, 4H), 4.07 (t, 4H), 1.78 (q, 4H), 1.43 (m, 4H), 1.26 (m, 20H), 0.87 (t, 6H). ¹³C NMR (400 MHz, DMSO-d₆) ppm: δ 161.79, 160.38, 151.24, 146.60, 135.48, 126.76, 124.86, 123.09, 115.47, 68.42, 31.73, 29.52, 29.41, 29.21, 29.08, 25.93, 22.62, 14.48

Acknowledgements: Authors are gratefully thankful for the technical support from National Research Centre, Cairo, Egypt.

References

1. Neal K. Devaraj, Ralph Weissleder, and Scott A. Hilderbrand. "Tetrazine-based cycloadditions: application to pretargeted live cell imaging." *Bioconjugate chemistry* 19, no. 12 (2008): 2297-2299.
2. Neal K. Devaraj, and Ralph Weissleder. "Biomedical applications of tetrazine cycloadditions." *Accounts of chemical research* 44, no. 9 (2011): 816-827.
3. V. P. Krivopalov, M. B. Bushuev, Yu V. Gatilov, and O. P. Shkurko. "Synthesis of symmetrical di (pyrimidin-2-yl)-1, 2, 4-triazoles and di (pyrimidin-2-yl)-1, 2, 4, 5-tetrazines." *Russian Chemical Bulletin* 59, no. 9 (2010): 1808-1816.
4. Gilles Clavier, and Pierre Audebert. "s-Tetrazines as building blocks for new functional molecules and molecular materials." *Chemical reviews* 110, no. 6 (2010): 3299-3314.
5. Yong-Hua Gong, Fabien Miomandre, Rachel Méallet-Renault, Sophie Badré, Laurent Galmiche, Jie Tang, Pierre Audebert, and Gilles Clavier. "Synthesis and Physical Chemistry of s-Tetrazines: Which Ones are Fluorescent and Why?." *European Journal of Organic Chemistry* 2009, no. 35 (2009): 6121-6128.
6. R. G. Dickinson, and N. W. Jacobsen. "A new sensitive and specific test for the detection of aldehydes: formation of 6-mercapto-3-substituted-s-triazolo [4, 3-b]-s-tetrazines." *Journal of the Chemical Society D: Chemical Communications* 24 (1970): 1719-1720.
7. Patrick Roffey, and John P. Verge. "Some reactions of 3, 6-disubstituted-s-tetrazines; A new synthesis of the 1, 2, 4-triazine ring system." *Journal of Heterocyclic Chemistry* 6, no. 4 (1969): 497-502.
8. Yingjie Zhao, Yongjun Li, Zhihong Qin, Runsheng Jiang, Huibiao Liu, and Yuliang Li. "Selective and colorimetric fluoride anion chemosensor based on s-tetrazines." *Dalton Transactions* 41, no. 43 (2012): 13338-13342.
9. S. A. Lang Jr, B. D. Johnson, E. Cohen, A. E. Sloboda, and E. Greenblatt. "Aryl-s-tetrazines with antiinflammatory activity." *Journal of medicinal chemistry* 19, no. 12 (1976): 1404-1409.

10. H. H. Takimoto, and G. C. Denault. "3-Amino-s-tetrazines from the thermal decomposition of 4-amino-3-azido-s-triazoles." *Tetrahedron Letters* 7, no. 44 (1966): 5369-5373.
11. Waluk, Jacek, Jens Spanget-Larsen, and Erik W. Thulstrup. "Electronic states of symmetrically disubstituted s-tetrazines." *Chemical physics* 200, no. 1-2 (1995): 201-213.
12. Tawfik A. Khattab, "Synthesis and Self-assembly of Novel s-Tetrazine-based Gelator." *Helvetica Chimica Acta* 101, no. 4 (2018): e1800009.
13. Melissa L. Blackman, Maksim Royzen, and Joseph M. Fox. "Tetrazine ligation: fast bioconjugation based on inverse-electron-demand Diels–Alder reactivity." *Journal of the American Chemical Society* 130, no. 41 (2008): 13518-13519.
14. Dale L. Boger, and Scott E. Wolkenberg. "Total synthesis of Amaryllidaceae alkaloids utilizing sequential intramolecular heterocyclic azadiene Diels–Alder reactions of an unsymmetrical 1, 2, 4, 5-tetrazine." *The Journal of organic chemistry* 65, no. 26 (2000): 9120-9124.
15. Subas M. Sakya, Kelley K. Groskopf, and Dale L. Boger. "Preparation and inverse electron demand Diels-Alder reactions of 3-methoxy-6-methylthio-1, 2, 4, 5-tetrazine." *Tetrahedron letters* 38, no. 22 (1997): 3805-3808.
16. Jianfu Ding, Naiheng Song, and Zhao Li. "Synthesis, characterization and photovoltaic applications of a low band gap polymer based on s-tetrazine and dithienosilole." *Chemical Communications* 46, no. 45 (2010): 8668-8670.
17. Xiaowu Yu, Yanhua Luo, Wenxuan Wu, Qing Yan, Gang Zou, and Qijin Zhang. "Synthesis and reversible thermochromism of azobenzene-containing polydiacetylenes." *European Polymer Journal* 44, no. 9 (2008): 3015-3021.
18. Roxana Judele, Sabine Laschat, Angelika Baro, and Manfred Nimtz. "Gallic esters of 4, 5-dinitrocatechol as potential building blocks for thermotropic liquid crystals." *Tetrahedron* 62, no. 41 (2006): 9681-9687.
19. Jaroslaw Spsychala, "4-(cyclic amidino) phenols-Preparation and use in a diamidine synthesis." *Synthetic Communications* 30, no. 6 (2000): 1083-109.

(Received 4/9/2018 ;
accepted 26/9/2018)

توليف وتوصيف صبغة ثنائي الازو تيترازين

توفيق خطاب * ومحمد ريجان

شعبة بحوث الصناعات النسيجية ، المركز القومي للبحوث ، القاهرة ، مصر

تم تحضير وتوصيف مركب ثنائي الازو تيترازين متماثل التركيب الجزيئي وذلك من خلال تفاعل إضافة بين مركب ديسيلوكسبيل فينيل ديازبنيل بنزونترييل مع هيدرازين هيدرات ثم اجراء عملية أكسدة. تم التحقق من التركيب الجزيئي بواسطة تقنيات تحليلية مختلفة تشمل التحليل الطيفي بالأشعة تحت الحمراء ، تحليل العناصر والرنين النووي المغناطيسي.