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SYNTHESIS AND CHARACTERIZATION OF NEW COMPLEX HETEROCYCLIC RING SYSTEMS OF INDUSTRIAL IMPORTANCE

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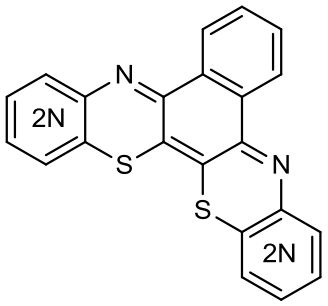
Abstract

The synthesis and characterization of new complex monoaza and pentaaza angular phenothiazine derivatives is reported. The first derivative, 6,10-Dichloro-17-azadibenzo[a,n]triphenodithiazin-5,11-dione**10** was obtained by a base-catalyzed reaction of 2,6-diaminopyridine-3,5-dithiol **5**and 2,3-dichloro-1,4-naphthaquinone **9**, while that of the second derivative, 7,9,15,17-tetraamino-6,8,16,18,25-pentazadibenzo[a,n]di([1,4]benzothaizino[3,2-c,l])triphenodiathizine (**11**) was achieved by the reaction of two moles of 2, 4, 6-triaminopyrimidine-3-thiol (**8**) and one mole compound (**10**) under the same reaction conditions.. The assigned structures to the above synthesized compounds were done on the basis of spectroscopic analysis.

Keywords: Monoaza, Pentaaza, Triphenodiathiazin, Triaminopyrimidine-3-thiol, Phenothiazine.

1. Introduction

The search for active chemical compounds that can be used for the production of drugs to combat many of the diseases plaguing mankind is ongoing. Most of these compounds are heterocyclic of which phenothiazine and its numerous derivatives are not left out. Apart from the medicinal and biological importance [1] [2] [3], phenothiazine derivatives are useful in agricultural, textile, paint, petroleum, pharmaceutical industries etc. [4], for the production of pesticides, dyes and pigments, antioxidants, drugs and many other pharmaceutical products [4] [5] [6] [7]. There are few reports on the synthesis of phenothiazine derivatives of the type **1**.However, Ezema and co-workers [8] reported the synthesis of phenothiazine derivative of the type **1**. At the moment, there is little or no report on the synthesis and chemistry of phenothiazine derivatives of the type **2**. In this write up, we present the synthesis and characterization of this useful heterocyclic compound.



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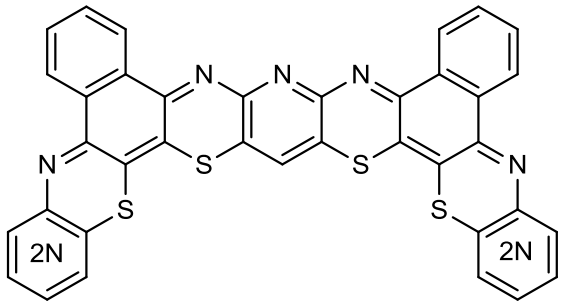

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2. Experimental Procedure

The melting points of all the synthesized compounds were determined with a Fisher John apparatus and are uncorrected. UV/Visible spectra were recorded on a Pye- Unicam SP 800 spectrophotometer using matched 1cm quartz cells; IR spectra in KBr on a Perkin Elmer 137 spectrophotometer; ^{1}HMNR spectra on a Varian Associates T – 60 instrument (chemical shift are reported on the δ scale relative to tetramethylsilane (TMS) as internal standard).Analytical samples were obtained by column chromatography on aluminum oxide 90(Merck, 70 – 230 mesh ASTM) using acetone and benzene(1:1) as an eluent before recrystallization.

Compounds **5** and **10** were prepared as previously reported in the literature [9] [10].

2.1 2, 4, 6-Triamino-3-thiocyanatopyrimidine (7)

2, 4, 6-Triaminopyrimidine **6** (5.50g, 0.0413mole), potassium thiocyanate (5.0g,0.526mole) and precooled acetic acid (100ml) were placed in a two neck flask equipped with a mechanical stirrer, and the mixture was stirred for 30 minutes. Bromine (5ml) in a precooled acetic acid was the added intermittently using thistle funnel. The addition of bromine took about 2hours.After the addition of bromine the mixture was stirred for another two hours always maintaining a temperature between -5^{o}C and 0^{o}C. After this, the mixture was stirred for additional 10 hours at room temperature and then the slurry left to stand overnight. Boiled water (50ml) was later added to the mixture and then filtered hot. The residue was washed with acetic acid (50ml) and water (50ml) respectively and added to the filtrate and neutralized with concentrated ammonia to a pH of 9 not allowing the temperature to exceed 20^{o}C.The yellow precipitate formed was filtered, dried and recrystallized with acetone to yield compound **7** (8.50g, 70%),m.p< 200^{o}C,as described previously [10].

2.2 2,4,6-Triaminopyrimidine-3-thiol (8)

2,4,6-Triamino-3-thiocyanatpyrimidine **7** (9.0g, 0.0672mole) was placed in a 250ml two-necked flask equipped with refluxing apparatus. Potassium hydroxide (15.50g, 0.2768mole) in water was added and the content of the refluxed for 30h in a sand bath until ammonia gas stops evolving. At the end of the reaction, the mixture was allowed to cool and neutralized with acetic acid in a sand bath, maintaining a temperature below 20^{o}C in the process. a massive yellow precipitate was formed and was filtered, dried and recrystallized from acetone to give compound **8** in good yield as a crystalline product (6.8g 60%),m.p. > 260^{o}C. UV-Vis (EtOH) λ_{max}(nm) (ε): 248(2.7499), 325(3.6037), 390(4.3244); IR (KBr):ν_{max} 3385cm^{-1} (3NH), 1532CM^{-1} (C=C, C=N), 779, 740,660cm^{-1}. ^{1}HNMR (DMSO-d_6): δ 9.40 (s,3NH_2) and δ 6.13 (s,SH); ^{13}CNMR(DMSO-d_6)(ppm): 163.142(3C-NH_2),and 125.121(C-SH).

2.3 7,9,15,17-Tetraamino-6,8,16,18,25-pentaazadibenzo[a,n]di-([1,4]-benzothiazino-[3,2])-[c,l]triphenodithiazine (11)

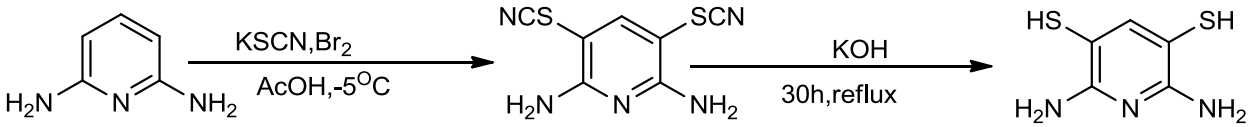
A mixture of 2,4,6-tiaminopyrimidine-3-thiol **8** (5.0g, 0.0472mole) and anhydrous sodium carbonate(2.50g, 0.0236mole) was place in a 250ml 3- necked reaction flask equipped with a magnetic stirrer, thermometer, and reflux condenser. A solution of DMF (5ml) and benzene (50ml) was added and the mixture reflux for 30 minutes. 6, 10-dichhloro-17-azadibenzo [a,n]triphenodithiazin-5,11-dione **10** (2.50g, 0.00483mole) was added to the mixture and

content of the flask was refluxed in a water bath with continuous stirring for 8h. At the end of the reaction, benzene was distilled and water was added to the slurry and heated boil for 2min, filtered, dried and subjected to column chromatography on aluminum oxide employing benzene and acetone as eluent. The product was later recrystallized from acetone to obtain the above compound **11** a reddish crystalline substance (3.65g, 60%) m.p. >300^{o}C.

UV-vis:(nm)(ε) 420(4.6571), 525(5.8214), 600(6.6530); IR: 3402cm^{-1} (>N-H), 2951cm^{1},1525cm^{-1}, 790cm^{-1} ,724cm^{-1}; ^{1}HNMR(DMSO-d_6) δ: 9.89(8H,m,4NH_2), 8.76(8H,m,Ar-H), 7.00(s,12-H); ^{13}CNMR(DMSO-d_6): (ppm) 160.10(4C), 150.12(1C). 145.25(8C), 142.20(5C), 14021(4C), 139.32(3C), 138.10(3C), 137.6094C)

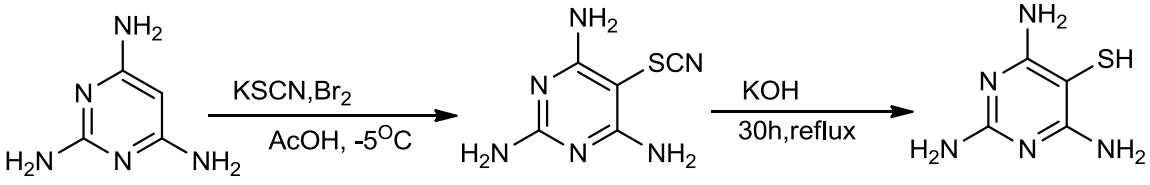
3. Results and Discussion

The key intermediate 2, 6-diaminopyridine-3, 5-dithiol **5** was obtained by the thiocyanation of 2, 6-diaminopyridine **3** to give 2,6-diamino-3,5-dithiocyanatopyridine **4** which underwent hydrolysis with potassium hydroxide to furnish compound **5** [9][10].



3 4 5

The second key intermediate, 2,4,6-triaminopyrimidine-3-thiol**8** was also obtained using a similar method as stated above. Here, 2,4,6-triaminopyrimidine **6**was subjected to thiocyanation to give 2,4,6-triaminothiocyanatopyrimidine**7** which was later hydrolyzed using potassium hydroxide to furnish the product **8** in good yield. [10].



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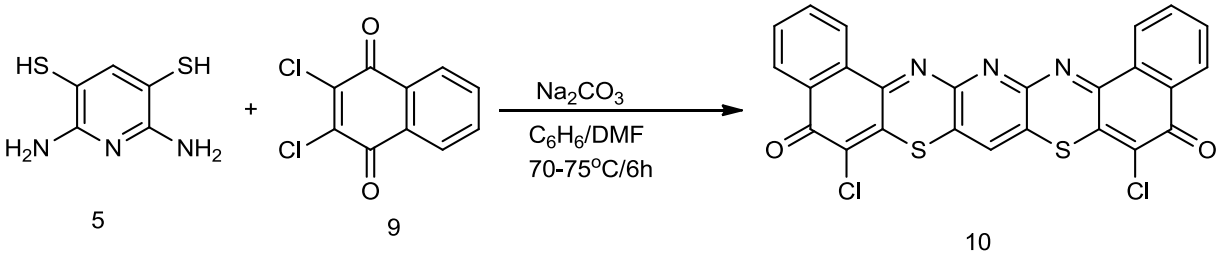
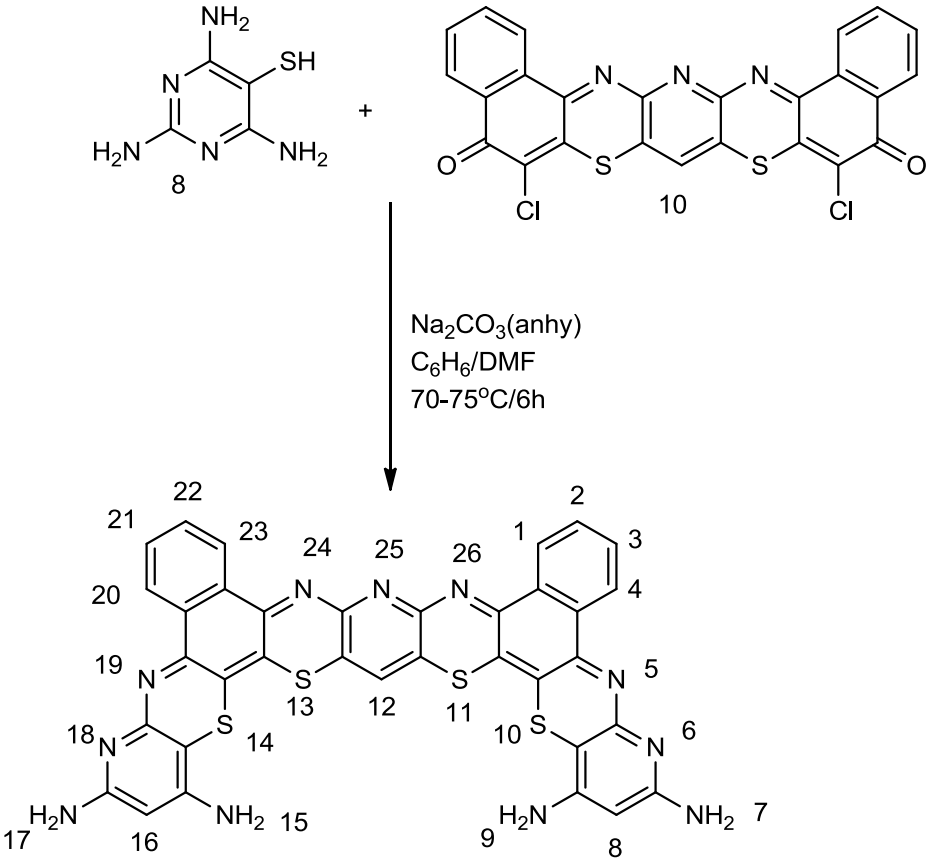
. The condensation of equimolar amount of compound **5** with 2,3-dichloronaphthoquinone**9** in an alkaline medium yielded 6, 10-dichloro-17-azadibenzo[a,n]triphenodithiazin-5,11-dione **10,**in good yield [10] [11].



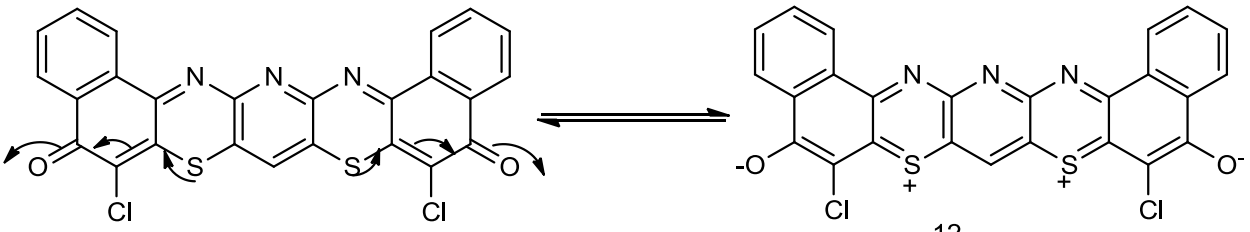
5 9 10

The presence of the active halide atoms at 6th and10th positions as well as the carbonyl groups at the 5thand 11th positions of compound **10** above, provided reaction sites for the second reaction with two moles of 2,4,6-triaminopyrimidine-3-thiol **8** to give 7,9,15,17-tetraamino-6,8,16,18,25-pentaazadibenzo[a,n]di([1,4]benzothiazino[3,2])-[c,l]triphenodithiazine.



The structures of the above synthesized compounds agreed with the microanalyses of both[1]HNMR and [13]CNMR.The proton NMR revealed peaks at δ7.06(singlet, 8-H) and 8.90 (multiplets benzenoid protons).In the [13]CNMR spectrum, the signals at 190.52ppm(singlet) representing the two carbonyl carbons,160.15ppm(singlet) represent the carbon atoms at the 6th and 10th positions of the above compound,151.61ppm(singlet) stands for C-8 while 141.34-139.43ppm (multiplets) stands for all other benzenoid carbons. The UV-vis spectrum of compound **10** revealed signals at 370nm (ε = 3.9919),500nm (ε = 4.1582) and 593nm (ε = 4.9233).The IR spectrum showed peaks at 2950cm^{-1}(C-CH stretching), 1680cm^{-1} due to the

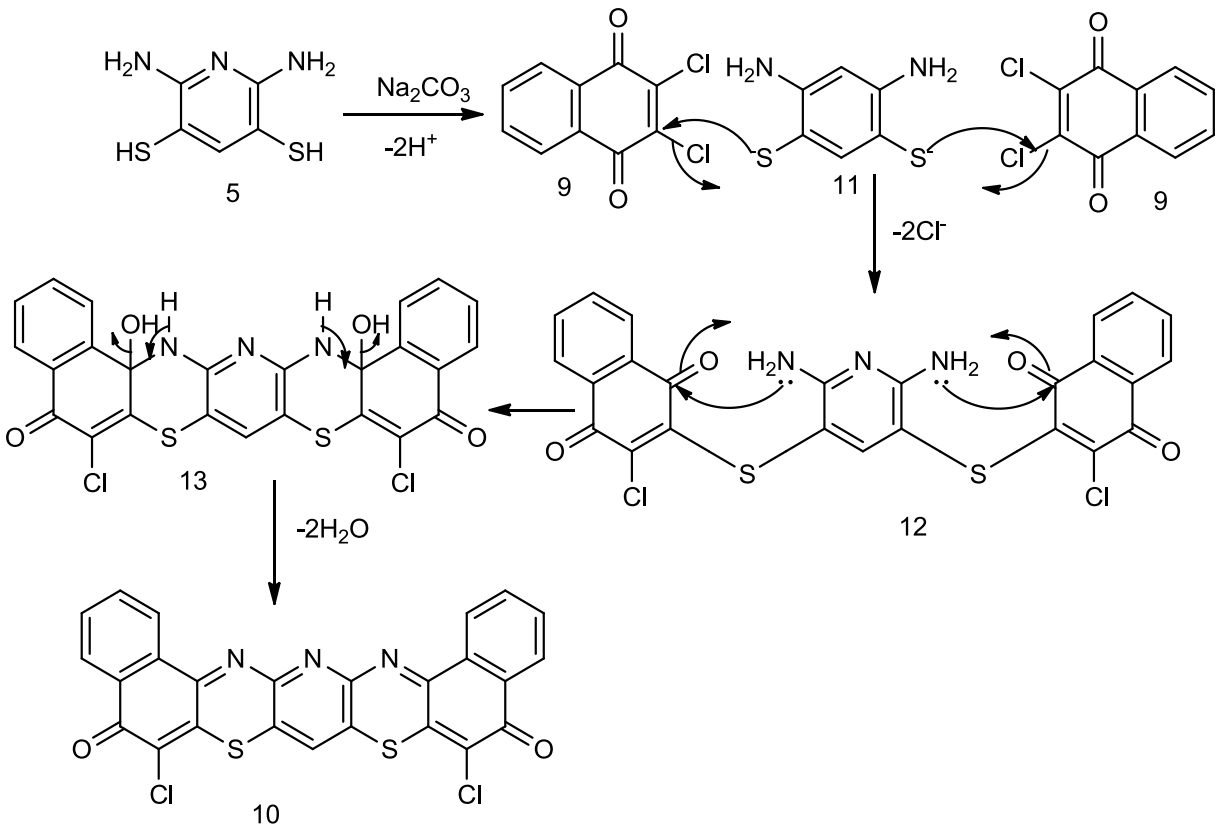
carbonyl groups,1540cm^{-1} (C=C,C=N stretching),780cm^{-1} (for a 1,2-disubstituted benzene rings). However, a lowering in the carbonyl absorption band was observed, from the expected 1730cm^{-1} to 1680cm^{-1} as a result of the contribution of the ionic structure **12** to the resonance stability of the compound **10** as shown below[10] [11] .



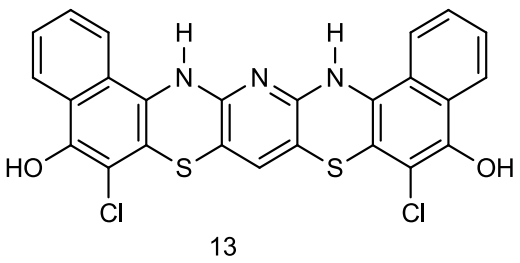
10 12

The ^{1}HNMR spectrum of compound **11** showed signals at δ9.89 (multiplets) representing the eight N-H protons, 8.76(multiplets), for all the eight benzenoid(C-1,2,3,4,20,21,22 and23) protons, 7.00(singlet) for the proton at C–12.The^{13}CNMR spectrum gave no signal at 170-200ppm which explains the absence of the carbonyl carbons. This is consistent with the assigned structure. However, signals were observed at 160.10ppm (multiplets) for C-7, 9, 15 and 17, the signal at 150.02(a singlet) is assigned to C-12, while the signals at 145.25-137.60 (multiplets) is for the remaining carbon atoms of the above compound. The absence of absorption at 1970-1650 cm^{-1} for the carbonyl group in the IR spectrum of compound **11** further supported the assigned structure. The absorption bands at 420nm, 525nm and 680nm in the visible region showed that there is extension in conjugation, hence the violet color of the compound.

The non-linear azaphenothiazine-5,11-dione **10** is formed by the nucleophilic attack of the mercaptide diions **11** on C-3 of the 2,3-dichloro-1,4-naphthoquinone molecules **9** leading to the loss of two moles of Hydrogen chloride [10] [11 [12]. Condensation of the appropriate naphthoquinone carbonyl groups with amino groups in the pyridine moiety led to the isolation of **10**.



Reduction of compounds **10** and **11** to their corresponding leuco-bases forms of **13** and **14** using sodium hydrogen sulphite was also achieved; nevertheless, these derivatives were unstable and could not be isolated. They reverted to the dehydro forms which are highly colored quinonoid compounds **10** and **11**, when exposed to air. The oxidation was however, facilitated by the use of hydrogen peroxide. This property as well as their high melting points makes them applicable as vat dyes and pigments [12][13] [14].



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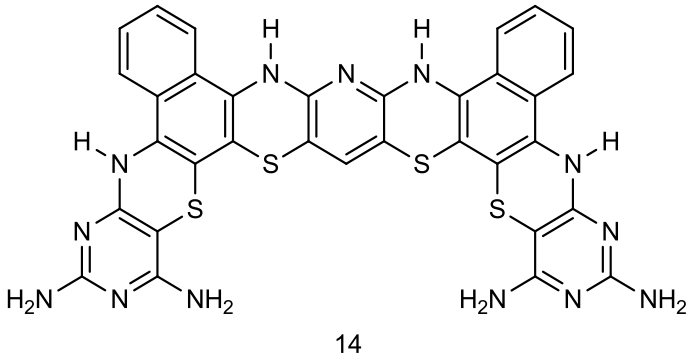

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4. Conclusion

The synthesis of phenothiazine derivatives discussed above was carried out using simple commercially available starting materials. The methods employed are straight forward and

stereo-selective products were obtained. These newly synthesized compounds have promising and interesting applicability in pharmaceutical, textile, petroleum, agricultural industries etc.

The intense colors of these compounds suggest that they could be used as dyes. Studies on their dyeing and antimicrobial potentials are ongoing in our laboratory.

5. Acknowledgement

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