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Synthesisand Characterization of 6–(4-Bromophenyl)-10-methyl-11-azabenzo[a] phenothiazin-5-one

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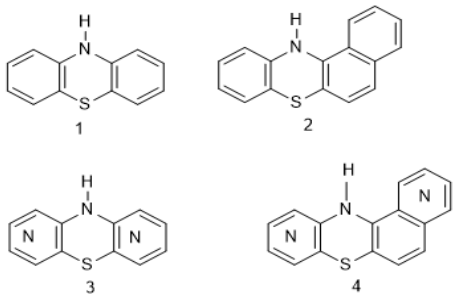
Abstract The synthesis of a new derivative of a non-linear azaphenothiazine of industrial importance, 6-(4-bromophenyl)-10-methyl-11-azabenzo[a]phenothiazin-5-one is reported. This was obtained via transition metal catalyzed cross coupling reaction. Alkaline hydrolysis of 2-amino-6-methyl thiozole [4,5b] pyridine in 20% sodium hydroxide solution and neutralization with acetic acid yielded 2-amino-6-methylpyridine-3-thiol. Base catalyzed (anhydrous Sodium carbonate) condensation of 2,3-dichoro-1,4-naphthoquinone and 2-amino-6-methylpyridine-3-thiol gave 6-chloro-10-methyl-11-azabezo[a]phenothiazin-5-one which coupled with 4-bromophenyl boronic acid in the presence of a transition metal catalyst system to furnish the new phenothiazine derivative above. The ease of oxidation of these new heterocyclic compounds to the corresponding sulphoxide using hydrogen peroxide, suggest their applicability as antioxidants in lubricant and fuel. The stability of the iminoquinoid system is attributed to ionic resonance effect.

Keywords 6-(4-bromophenyl)-10-methyl-11-azabenzo[a]phenothiazin-5-one, Hydrolysis, Catalyst, 6-chloro-10-methyl-11-azabenzo[a]phenothiazin-5-one

1. Introduction

Studies in phenothiazine chemistry have gained wide acceptability over the years and different derivatives of this heterocyclic system both linear of the type **1** and nonlinear of the type **2** analogues have been synthesized and reported [1-4]. Although the linear azaphenothiazine analogues of the type **3** and the non-aza angular phenothiazine of the type **2** have been extensively studied [5], the angular aza phenothiazine of the type **4** and their derivatives have not been studied extensively.



Scheme 1

Due to their wide spectrum of pharmacological and biological activities, several of these derivatives are in clinical use [6-10]. The angular derivatives especially of the type **4** have so many industrial uses in the pharmaceutical, textile, paint, agricultural and petroleum industries [11]. Variation in the ring of these heterocyclic systems brings about a mark change in their biological activities [12]. In furtherance of the interest in this type of compounds, we have successfully synthesis 6-chloro-10-methyl-11-azabenzo[a]phenothiazine-5-one and 6-(4-bromophenyl)-10-methyl-11-azabenzo[a]phenolthiazin- 5-one.

2. Experimental

Melting points were determined with electro thermal melting points apparatus in open capillaries and are uncorrected. Uv and Visible spectra were recorded in DMF on a Jenway 6405 Uv/Vs spectrophotometer, using matched 1cm quartz cell. IR spectra in (KBr) on a FTIR (NARICT, Zaria), ^{1}H–NMR and ^{13}C-NMR on a JEOL Associate E-400 instrument (chemical shift are reported on the δ scale relative to tetramelthylsilane (TMS) as an internal standard) and mass spectra on a Shimadzu QP2010 spectrophotometer. Analytical samples were obtained by column chromatography on aluminum oxide 90 (Merck, 70–230 Mesh ASTM) employing benzene-chloroform (1:1) as

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eluting solvent before recrystallization. Compounds **6** and **7** were prepared as reported in the literature [13].

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2-Amino-6-methylpyridine-3-thiol **7** (0.40mole) was placed in a reaction flask containing benzene (50ml) and DMF (5ml). Anhydrous sodium carbonate (0.020mole) was added and the mixture heated (reflux) at 70–75°C with stirring for 45 minutes. 2,3-didiloro-1,4-naphthoquinone **8** (0.027mol) was then added and the mixture was heated under reflux for 6h. At the end of the refluxing period, the resulting reddish brown liquor was poured onto crushed ice (200g) and stirred. The resulting solid was filtered and treated with water to precipitate the clean product. This was dried and subjected to column chromatography using a mixture of benzene and chloroform (1:1) as eluting solvent followed by recrystallization, to furnish compound **9** (6.60g) m.p › 190°C. Uv– Visλmax 327 (ε=1.844) nm, 343 (ε=1.934)nm. IR (KBr), 1672cm^{-1} (C=O), 3097cm^{-1}(C –H stretching), 1559cm^{-1} (C=N of pyridine), 845cm^{-1}.^{1}H-NMR (DMSO-d_6) δ 8.29 (s,10-H), δ 8.09 (d,8-H and 9-H), δ 7.19 (m,4H,Ar), 2.25 (s,methyl protons); ^{13}C-NMR (DMSO-d_6) δ:176.13 (carbonyl carbon,1C,s), 142.37) (6C, m), 137.80(5C, m), 35.10 (CH_3,1C,s).

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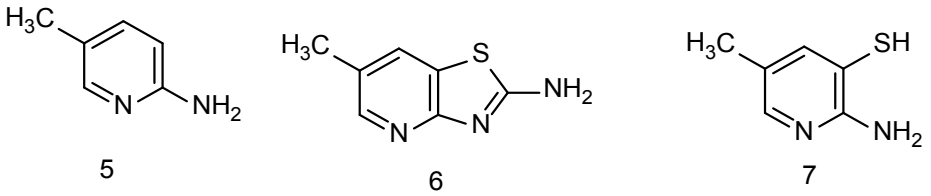
Diphenylphosphinobutane palladium chloride, Pd(dppb)$_2$Cl ((0.005mol),1,4-bis-(2-hydroxy-3,5-di-*tert*-butylbenzyl) piperazine(0.005mmol) and mixture of DMF and toluene (10ml) (2:3) were placed in a 250ml two- necked round bottom flask and stirred for 5min. with a short magnetic bar without heat. After 5 minutes of stirring 6-chloro-10-methyl-11-azabenzo[a]phenothiazin-5-one **9** (1.047mmol), 4-bromophenylboronic acid 15(0.75mmole), potassium carbonate (1mmole) were added and the mixture refluxed at 120°C for 24h. At the end of the reaction, the mixture was placed in a 250ml beaker and treated with crushed ice (200g), the solid was filtered and treated with water (20ml) to obtained the clean product. The residue was allowed to dry and recrystallized from acetone to obtain compound **15**, a reddish brown powder, m.p >125°C.

Uv-vis: λmax, 321 (ε=1.910) nm, 410(ε=2.312)nm; IR (KBr), 3018cm^{-1},2950cm^{-1} (C-H streching), 1668cm^{-1}(C=O), 1580cm^{-1}, 1469cm^{-1}, 825cm^{-1}; MS: *m/z* (relative intensity) 434(M^+100%), 402(M^+-S)25%, 353(M^+-Br)15%, 277(M^+-C_6H_4Br) 20%, ^{1}H-NMR(DMSOd_6)δ: 8.90 (s,C-10H), 8.05 (s,C-8H and C-9H) ,7.90 (d,4H,para substituted), 7.50 (m,4H,aromatic protons), 1.80 (s,methyl protons).

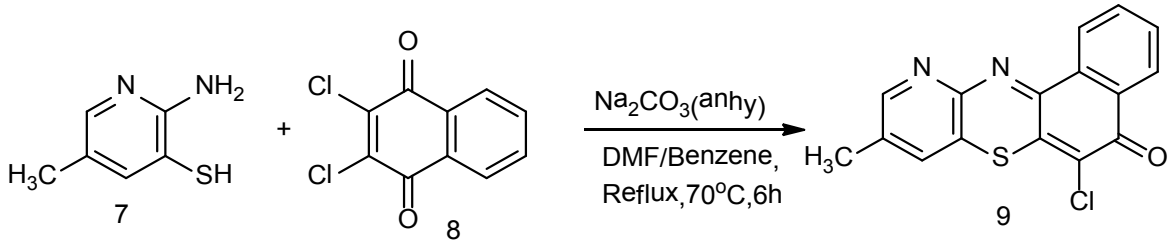
3. Results and Discussion

2-Amino-6-methylpyridine **5** was treated with potassium thiocyanate and bromine in acetic acid at 0°C followed by neutralization with concentrated ammonia to give 2-amino-6-methylthiozole [4,5b] pyridine **6** which was converted to 2-amino-6-methylpyridine-3-thiol **7** by alkaline hydrolysis [13].



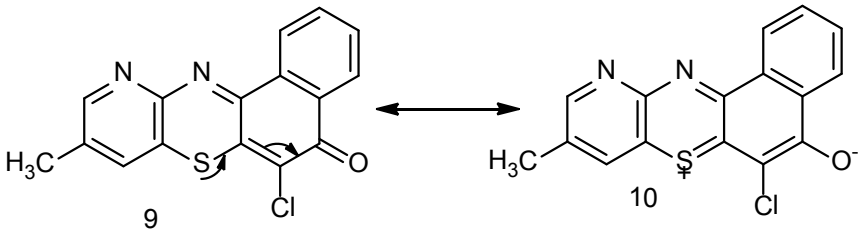
Scheme 2

Base catalyzed condensation of **7** and 2,3-dichloro-1,4-naphthoquinone **8** in small amount of DMF and benzene gave 6-chloro-10-methyl-11-azabenzo[a]phenothiazine-5-one **9**.



Scheme 3

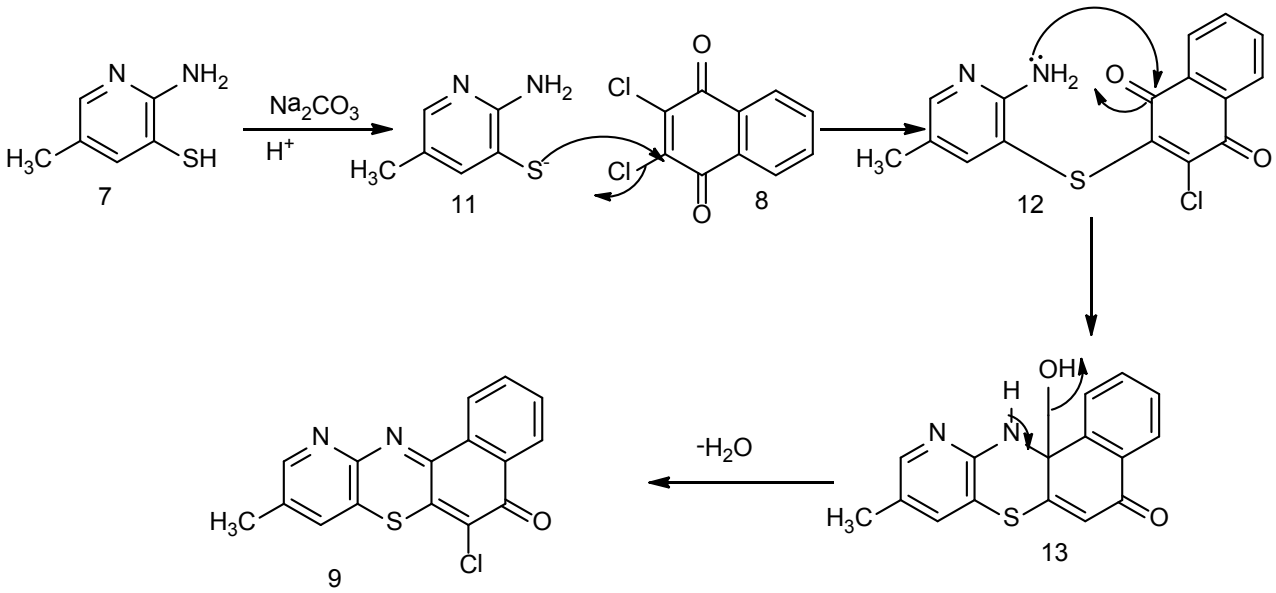
^{1}H-NMR, ^{13}C-NMR and IR spectra analysis are in agreement with the assigned structure **9**. The stability of the new heterocyclic iminoquiniod system **9** was due to ionic resonance effect, with the ionic resonance form **10** contributing to the ground state [13].



Scheme 4

There was a lowering of the carbonyl (C=O) absorption in the IR spectrum from the expected 1730cm[1] to 1665cm^{-1} due to the contribution of the ionic resonance in **10** which increased the (C=O) bond length in **9** with the attendant decrease in the vibration frequency of absorption as shown above.

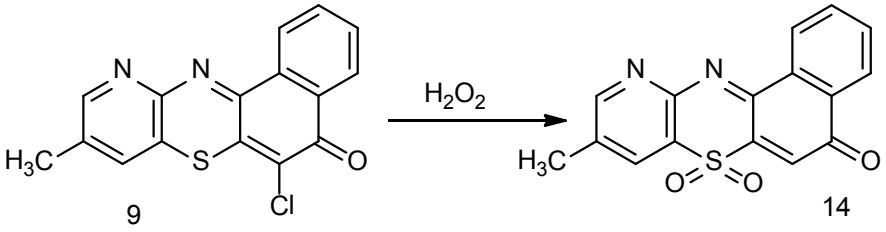
The non-linear azaphenothiazine-5-one **9** is formed by the nucleophilic attack of the mercaptide ion **11** on C-3 of the 2,3-dichloro-1,4-naphthoquinone **8** leading to the loss of sodium chloride. Condensation of the appropriate naphthoquinone carbonyl with amino group in the pyridine moiety led to the isolation of **9**.



Scheme 5

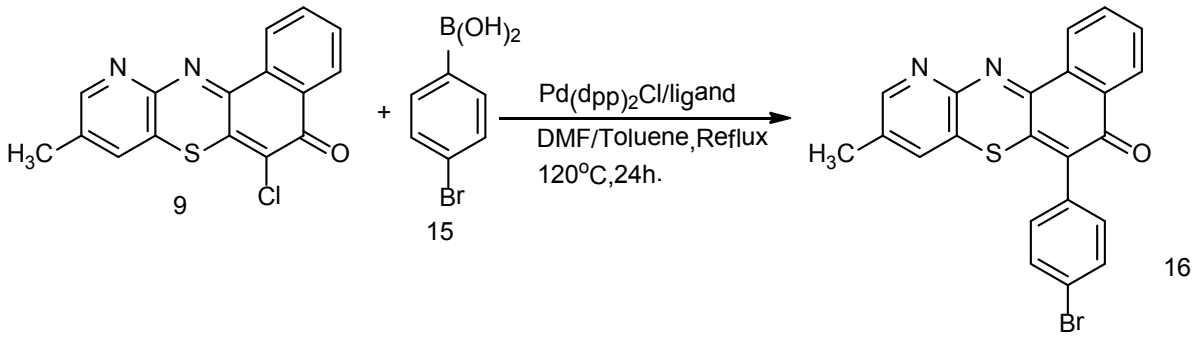
Treating compound **9** with (1:1) molar ratio of 30% H_2O_2 converted it to the sulphoxide.

The ease of the oxidation of compound **9** to sulphoxide suggests that it can be used as an antioxidant in lubricants and some petroleum products [14].



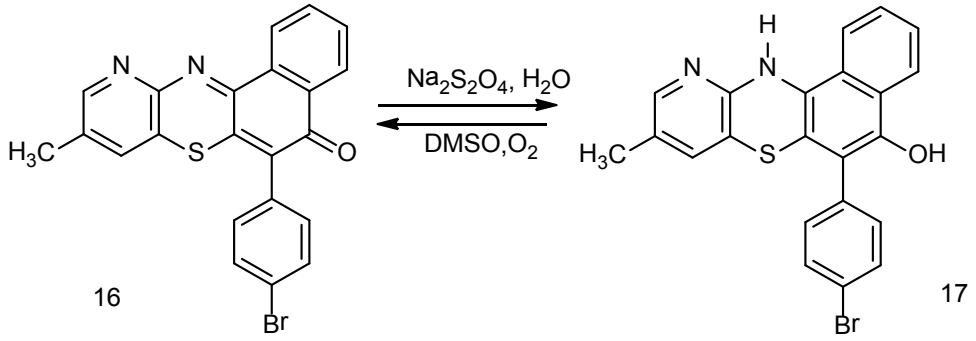
Scheme 6

Treatment of compound **9** with 4-bromophenyl boronic acid **15** in the presence of a palladium catalyst complex [15] gave 6-(4-bromophenyl)-10-methyl-11-azabenzo[a]phenothiazine-5-one **16**. Microanalysis, IR and Mass spectroscopy are in agreement with the assigned structure. Uv-vis absorption of 410nm (ε =2.312) shows that there is an extension of conjugation.



Scheme 7

Treating compound **16** with sodium dithionite gave color discharged unstable base **17** which reverted in the presence of atmospheric oxygen to dehydro compound **16**. This property makes compound **16** suitable as a vat dye [16].



Scheme 8

4. Conclusions

From the above discussion, these newly synthesized compounds could be used as vat dyes in the textile and other allied industries. The structures assigned to them were well supported by spectroscopic data. Based on these analyses the molecular formulae of the compounds are **$C_{16}H_9N_2SOCl$** and **$C_{22}H_{13}N_2SOBr$** respectively. The biological potency of these compounds shall be reported in our subsequent research reports.

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