UNDER PEER REVIEW

Research Paper

Synthesis of 3-azoindoles

ABSTRACT

Aim: To synthesize 3-azoindoles by diazonium coupling of 1, 2-dimethylindole.
Azo compounds are an important class of organic colorants which consist of a conjugated chromophore azo (-N=N-) group in association with one or more aromatic or heterocyclic systems[1-2]. Azo dyes based on heterocyclic amines have higher tinctorial strength and give brighter dyeing than those derived from aniline-based diazo components. Literature survey reveals that not much work has been done on N-alkyl 3-azoindoles and their pharmacological activity. It was been considered worthwhile to synthesise N-methyl-3-azoindoles as part of our ongoing research on the development of novel synthetic route for pyrrolo(3,2-b)indoles. We herein report a simple procedure for the synthesis of 3-azoindoles.

Keywords: Azo-coupling, N-methyl-3-azoindoles, synthesis, electrophilic substitution

1. INTRODUCTION

It has been known for many years that azo compounds are the most widely used class of dyes due to their versatility in various fields such as the dyeing of textile fiber, the coloring of different materials, coloured plastics, biological-medical studies and advanced applications in organic synthesis[3-11].For the past two decades, heterocyclic coupling agents[12] have received a great deal of attention because of their excellent properties which are light fastness, good substantivity, good migration and brilliant shade. Some of them are pyrazolones, iminopyrazolones, pyridones, and pyrimidine.
Manuela et al[13] reported that heterocyclic azo dyes derived from 5-N,N-dialkylamino-2,2'bithiophene couplers could be used as thermally stable, solvatochromic probes which therefore find applications in electro-optical devices and sensors. Lee[14] et al. attempted to synthesize a range of temporarily solubilized disperse dyes which have a wider variety of colour by using the aromatic heterocyclic compounds such as pyridone and indole as coupling components. They claimed that the light fastness of the dyes was moderate and all the other fastness results were good to excellent. Furthermore, it has been reported that addition-curable phenolic resins functionalized with phenylmaleimide-system has improved the thermal characteristics and give good mechanical performance to composites. They are desirable for application in composites for thermo-structural applications.[15]

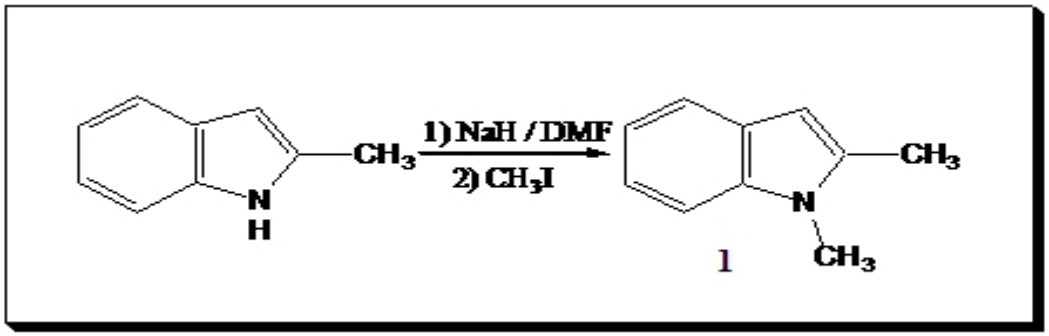
2. RESULTS AND DISCUSSION

Indole readily reacts with weak electrophilic reagents such as benzene diazonium ion[16]in neutral or alkaline media to give the azo coupled product at 3-position. Initially 1, 2-dimethylindole was prepared in 77% yield by methylation of 2-methyl indole by

UNDER PEER REVIEW

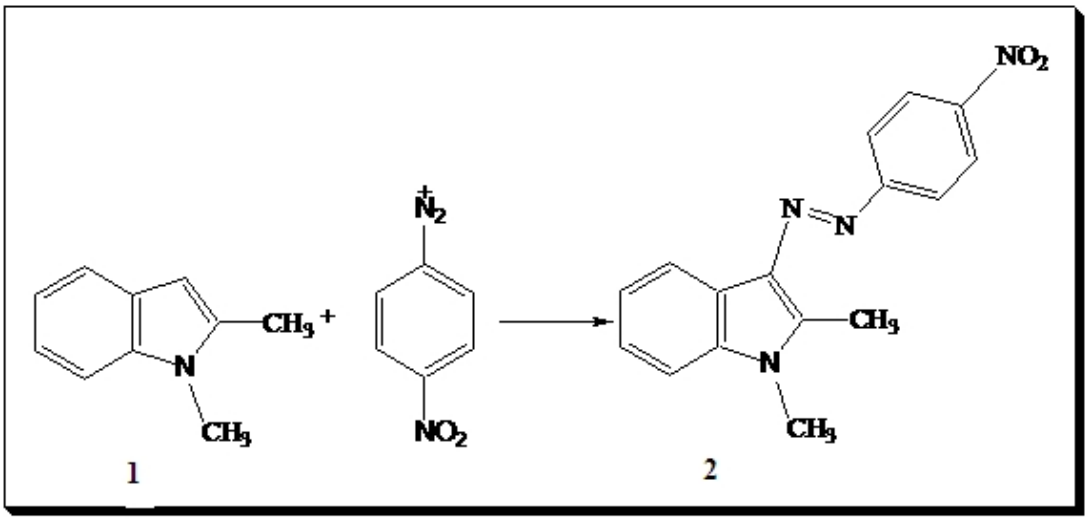
methyliodide using sodium hydride in DMF. The structure of the product was confirmed by its melting point, IR and NMR spectra.

Scheme:1 Synthesis of 1, 2-dimethylindole



Then, 1,2-dimethylindole (**1**) was coupled with diazotized p-nitro aniline to afford 1,2-dimethyl-3-(p-nitrophenylazo)indole (**2**) in 90% yield. The melting point, IR and NMR spectra (fig 1)were in accordance with the product structure.

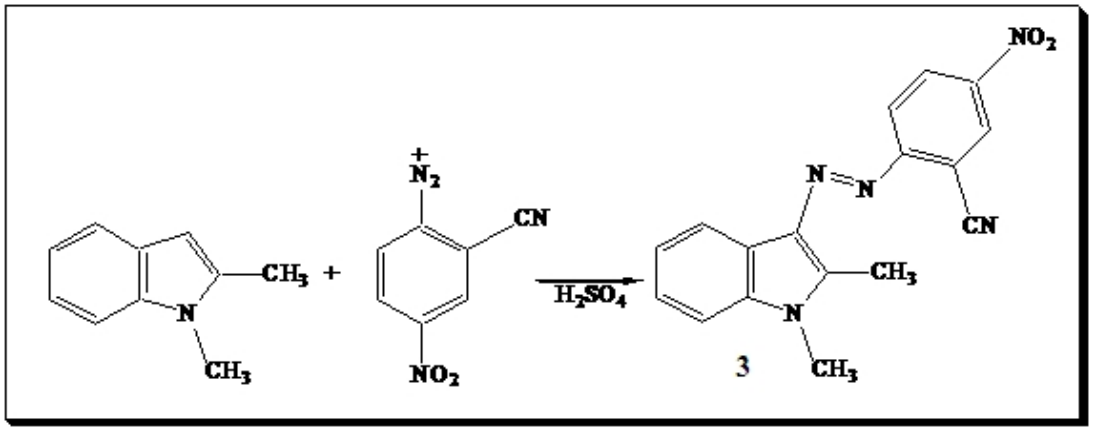
Scheme:2 Synthesis of 1,2-dimethyl-3-(p-nitrophenylazo)indole



The diazotization of 2-cyano-4-nitro aniline under the same conditions proved to be difficult. Finally it was found that the diazotiation of 2-cyano-4-nitro aniline proceeded with sodium nitrite and 50% sulphuric acid. The resulting diazonium salt was coupled with 1,2-dimethylindole to give the expected product namely 3-(2'-cyano-4'nitrophenylazo)-1,2-dimethyl indole (**3**) as a bright red solid in 85% yield. The structure of this novel azo coupled product has been confirmed by IR, NMR and elemental analysis data.

UNDER PEER REVIEW

Scheme:3 Synthesis of 3-(2'-cyano-4'nitrophenylazo)-1,2-dimethyl indole



The IR spectrum of this azo derivative showed bands at 2245 $^{cm-1}$due to cyano group, at 1342 and 1519^{cm-1} due to nitro group, and at 1645^{cm-1} due to C=N group. The 1H NMR spectrum exhibited a 3H singlet at δ 2.9 due to C-methyl hydrogens, a 3H singlet at δ 3.8 due to N-methyl hydrogen's, and a 7H multiplet at δ 7.1-8.7 due to aromatic hydrogens (Fig.2). Further the mass spectrum exhibited a molecular ion peak at *m/z* = 318.6 and base peak at *m/z* =143.9

3. EXPERIMENTAL

3.1 N-methylation of 2-methylindole

Synthesis of 1,2-dimethylindole (1)

To a well stirred suspension of NaH (2.4g, 100mmol) in dry DMF (80mL) at 00C was added a solution of 2-methylindole (13.1g, 100mmol) in dry DMF and the reaction mixture was stirred at 00 C under nitrogen atmosphere. After 0.5 h, methyl iodide (6.5mL, 100mmol) was added slowly and then stirred again for 6h. The reaction mixture was poured over crushed ice and the solid obtained was filtered and dried. It was purified by chromatography over silica gel using hexane as eluent.

Yield : 10g, (77%)

Mp : 550^{0}C (Lit[17]mp 55-580C)

3.2 Diazonium coupling of 1,2-dimethylindole with 2-cyano-4-nitroaniline

Synthesis of 1, 2-dimethyl-3-(p-nitrophenylazo)indole (2)

p-nitrophenyldiazonium salt was prepared from p-nitroaniline (0.759g, 5.5mmol) 30% hydrochloric acid (5mL) and sodium nitrite (0.380g,5.5mmol). Its pH was adjusted by the addition of sodium acetate followed by a solution of 1,2-dimethylindole (0.720g, 5mmol) in acetic acid (2mL) at 0-50C. After stirring for 30 min at this temperature the reaction mixture was stirred for 2 h at room temperature. The precipitated compound was collected by filtration and washed thoroughly with cold water and dessicated over anhydrous calcium chloride. It was recrystallized from ethanol.

Yield : 1.3g, (88%)

Mp : 206-209^{0}C dec (Lit[18]mp: 209-210^{0}C dec)

IR (KBr) : 1368, 1512 (NO2)

UNDER PEER REVIEW

^{1}H NMR (CDCl3/TMS) (200MHz): □□2.75 (s, 3H, CH_3) 3.8 (s, 3H, N-CH_3) 7.3-8.6 (m, 8H,Aromatic-H)

3.3 Diazonium coupling of 1,2-dimethylindole with 2-cyano-4-nitroaniline in acetic acid

Synthesis of 3-(2'-cyano-4'-nitrophenyl)azo-1,2-dimethylindole (3)

2-cyano-4-nitrophenyl diazonium salt prepared from 2-cyano-4-nitroaniline (0.902, 5.5mmol)50% sulfuric acid (10mL) and sodium nitrite (0.380g, 5.5mmol) in water was neutralized with sodium acetate and added to a solution of 1,2-dimethylindole (0.725g, 5mmol) in acetic acid(5mL) at 0-50C with stirring. After 30 min at this temperature the mixture was stirred for 2 h at room temperature. The red solid obtained was filtered and dried over anhydrous calcium chloride.

^{1}H NMR (CDCl3 /TMS): □□2.9 (s, 3H, CH3), 3.8 (s, 3H -CH3) 7.1-8.7(m, 7H, Aromatic-H)

Mass: m/z (%) : 318.6 (M+, 33.5), 171.9 (32.4), 143.9(100), 114.9 (29.8), 76.9(22.5), 57(9.3)

Analysis : C17H13N5O2	C	H	N
Calcd	*63.95*	*4.10*	*21.93*
Found	63.90	4.44	21.89

Yield : 1.24 g, (78%)

Mp : 260-264^{0}C

IR (KBr) : 2245(CN), 1342, 1519 (NO2)

Fig1: H^1 NMR spectrum of 1, 2-dimethyl-3-(p-nitrophenylazo)indole (2)

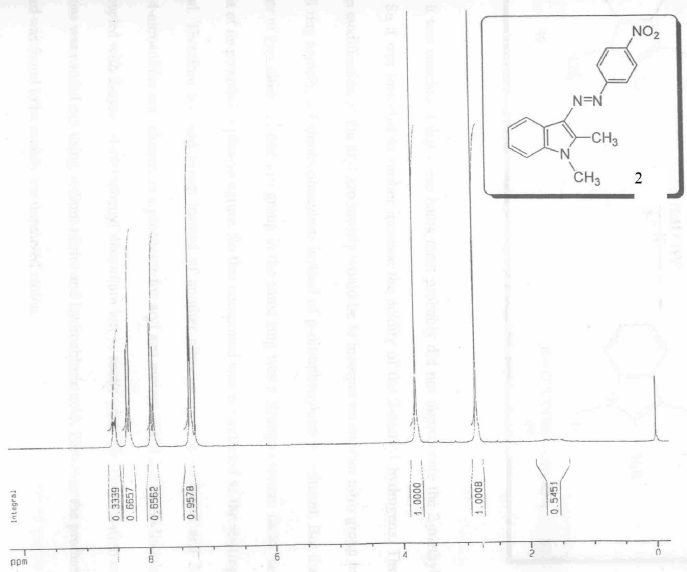
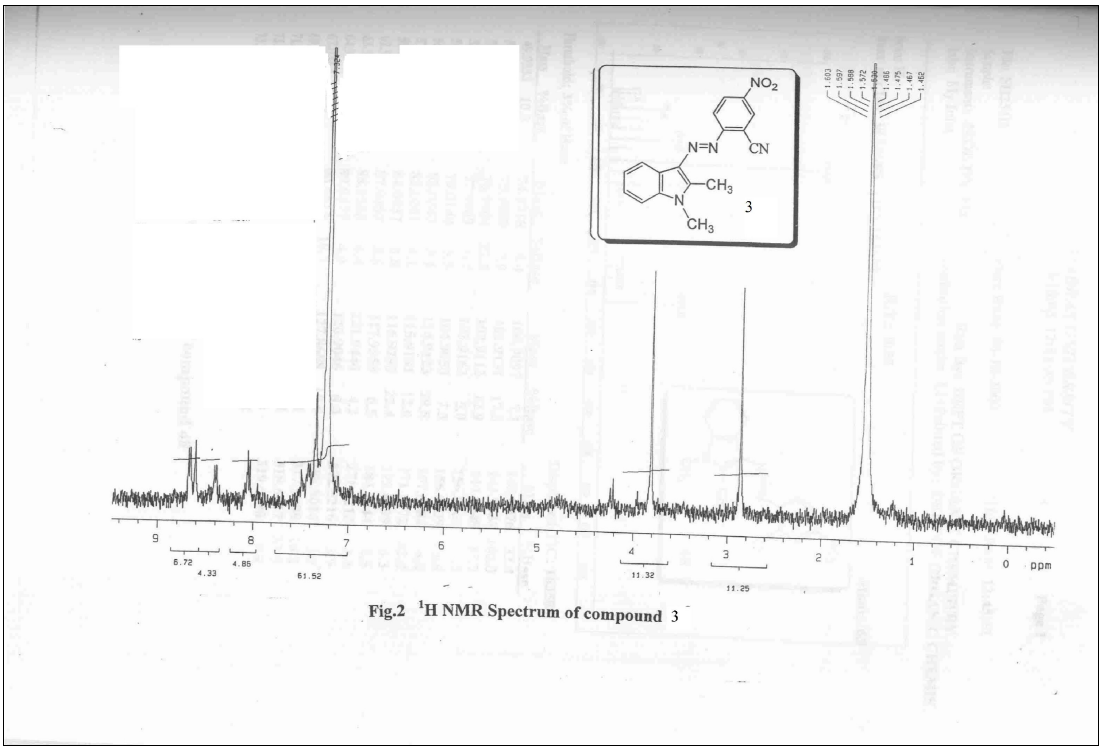


Fig.1 ^{1}H NMR Spectrum of compound 2

UNDER PEER REVIEW

Fig 2: H^1 NMR spectrum of 3-(2'-cyano-4'-nitrophenyl)azo-1,2-dimethylindole (3)



4. CONCLUSION

The above work presents a simple route for the synthesis of a novel 3-azo indole. We have synthesized and characterized a new heterocyclic azo dye **3-(2'-cyano-4'-nitrophenyl)azo-1,2-dimethylindole** by the coupling reaction of 2-cyano-4-nitrophenyldiazonium ion with 1,2-dimethylindole.

5. REFERENCES

1. Abrahart EN, Dyes and Their Intermediate. London: Pergamon Press. 1968.
2. Bindu RL, Reghunadhan Nair CP, Ninan KN, Journal of Applied Polymer Chemistry.2000; 38: 641-652.
3. Catino SC, Farris RE, In M. Grayson (ed.) *Azo Dyes*: Concise Encyclopaedia of ChemicalTechnology. New York: John Wiley and Sons. 1985.
4. Christie RM, Color Chemistry. United Kingdom: Royal Society of Chemistry. 2001.
5. Fadda AA, Etman HA, Amer FA, Barghout M, Mohammed K.S, Journal of Chemical Technology and Biotechnology. 1994; 61: 343-349.
6. Kocaokutgen H, Gumrukcuoglu I.E, Turkish Journal of Chemistry 1995; 19: 219-223.

UNDER PEER REVIEW

7. Hartman H,Schulze M, Guenther R. Dyes and Pigments.1991;15: 255-262.
8. Law K Y, Tarnawskyj IW, Lubberts, P. Journal of ImagingScience and Technology.1994; 38: 81-85.
9. Peters AT, Chisowa E. Dyes and Pigments, 1993;22: 223-238.
10. Tanaka K, Matsuo K, Nakanishi A,Jo M, Shiota H, Yamaguchi M, Yoshino S, Kawaguchi K. Chemical and Pharmaceutical Bulletin,1984; 32: 3291-3298.
11.Venkataraman K. The Chemistry of Synthetic Dyes.Vol. 3. New York: Academic Press.1970.
12. Schwander HR.Dyes and Pigments.1982; 3: 133-160.
13. Manuela MRM, Ferreira AMFP.; Pereira MMF, Belsley M, Moura JCVP. Dyes and pigments. **2009;**83:59-65.
14. Lee JJ, Lee W J, Kim JP.Fibers and Polymers. 2003**;** 4: 66-70.
15. Yang Y, Min Z, Yi L. Polymer Bulletin, 2007; 59:185-194.
16. Anthony H,Patrick P.L, J. Chem. Soc., Perkin Trans. 2, 1987; 1483-1488.
17. Noland WE, Kuryla WC, Lange RF.J. Am. Chem. Soc, 1959; 81; 6010.
18. Jackson A.H, Prasitpan N, Patrick VR, Shannon, Tinker AC. J. Chem. Soc. Perkin Trans.1, 1987; 11: 2543.