Chemistry and Materials Research
ISSN 2224- 3224 (Print) ISSN 2225- 0956 (Online)
Vol.7 No.4, 2015

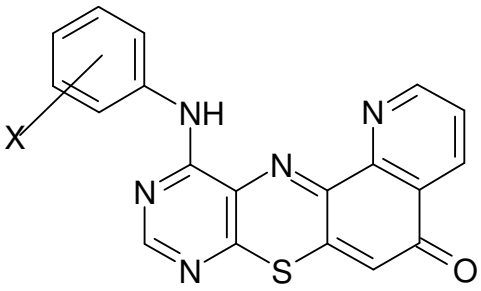
Copper Catalysed *N*-Arylation of Angular Triazaphenothiazinone

Ihejieto Anthony Ikenna[1], Okoro Uchechukwu Chris[2] and Jacob Alifa David[3*]
1. Department of Pure and Industrial Chemistry, University of Nigeria, Nsukka
2. Department of Pure and Industrial Chemistry, University of Nigeria, Nsukka
3. Department of Pure and Industrial Chemistry, University of Nigeria, Nsukka
* Email: alifajacob@gmail.com, alifa_david@yahoo.com

Abstract
The copper catalyzed *N*-arylation of angular aminotriazaphenothiazinone is reported. This was achieved by the coupling of 11-amino-1,8,10-triazabenzo[a]phenothiazin-5-one with potassium or lithium aryltriolborate in the presence of a copper catalyst for over 20h at room temperature to give the desired product. The success of this reaction lies in the preparation of the key intermediate, 11-amino-1, 8, 10-triazabenzo[a]phenothiazin-5-one synthesized by the condensation of 4, 5-diamino-6-thioprimidine with 7-chloro-5, 8-quinolinequinone in an anhydrous basic medium. Structures were assigned on the basis of spectral and analytical data.
Keywords: Aminotriazaphenothiazinone, triazabenzo[a]phenothiazinone, aryltriolborate, diaminothioprimidine.

1. Introduction

Phenothiazine belongs to an important class of heterocyclic compounds with a three-ring structure in which two benzene rings are joined by a sulfur and nitrogen atom at non-adjacent positions (Zhoa et al, 2001). The chemistry of phenothiazines has long been recognized by chemists for over a century and because of their usefulness in medicines, agriculture and industry, the synthesis of these compounds has remained unabated. In medicine, their derivatives are found to be useful as anticancer and antitumor agents (Kalkanidiz et al, 2002), they are also active components in sedatives, tranquilizers, antibacterial, antipsychotic and antimalarial agents (Mretzsch, 1954). Also in paints and plastic industries, they are used as pigments (Okafor et al, 1986) and in petroleum industries are useful as antioxidants in lubricants and fuels (Franz et al, 2009). Of recent, phenothiazines have become very useful in material science and in biochemistry as marker for proteins and DNA (Nakadan et al, 2005). They are also used as inodilators in congestive heart failures (Rang-Dale et al.,pharmacology, 6th edition). Owing to its wide range of applications, several research works have been carried out and still in progress in search for more derivatives with highly improved pharmacological and biological activities. These interests have been sustained and thousands of derivatives have been reported (Okafor et al, 1971). Also several reviews of its chemistry and application have appeared in the literature. Until about the mid-century, most of the reported derivatives of phenothiazines where side chains, which were of medical interest, but further research for more useful compounds have been reviewed in recent papers. This has lead to several reports describing successful synthesis of angular phenothiazines (Okafor et al, 1978) and their derivatives which are of use in both medical and industrial establishment (Okafor et al, 1986).
In a continued efforts in this direction, we now report the successful synthesis of more advanced derivatives of non-linear triazaphenothiazinone ring system of the type below**.**



Where X is H, 4-Br , 3-NO_2

2. Results and Discussions

The synthesis of derivatives of 11-amino -1,8,10-triazabenzo[a]phaothiazin-5-one was achieved by its coupling with potassium or lithium aryltriolborate for over 20 hrs in the presence of copper catalyst, at room temperature. The key to the synthesis of these derivatives lies in the successful preparation of the intermediate compound, 11-amino-1,8,10- triazaphenothiazin-5-one which was accomplished by the condensation of 4,5,diamino-6-thiopyrimidine with 7-Chloro-5,8-quinolinequinone in anhydrous basic medium. Elemental analyses and spectroscopy are consistent with the assigned structure

Table 1: Copper Catalysed N-Arylation of 11-amino-1, 8, 10- triazaphenothiazin-5-one

Entry	Substituted aryltriolborate	Product	Yield
1.	Phenyltriolborate	11-(Phenylamino)-1,8,10-triazabenzo[a] phenothiazin–5-one	70
2.	4-Bromophenyltriolborate	11-(4-Bromophenylamino)-1,8,10-triazabenzo[a] phenothazin–5-one	75
3.	3-Nitrophenyltriolborate	11-(3-Nitrophenylamino)-1,8,10-Triazabenzo[a] Phenothiazin-5-one	65

3. Experimental

3.1 General

The Melting points of the synthesized compounds were determined using electro thermal melting point apparatus in open capillaries and are uncorrected. Ultraviolet and visible spectra were recorded on Jenway 6405 UV/Vis spectrophotometer. Absorption maximum is given in nanometer (nm) and (logε) in parenthesis. Infrared spectra data were obtained on FTIR-8400S and absorption were in wave number (cm^{-1}). Nuclear magnetic resonance (^{1}H-NMR and ^{13}C-NMR) were determined on Variant 200MHz NMR machine and chemical shifts are reported in the δ-scale. Elemental analysis was carried out to determine the percentage abundance of elements present. All chemicals were bought from Zayo-Sigma (local vendor) and used as supplied.

3.2 11–Amino-1, 8, 10–Triazabenzo[a]Phenothiazin-5-one.

4,5-Diamino-6–thiopyrimidine (0.6g, 0.07mole) was suspended in benzene (40ml) and put into a 100ml 2-neck flask equipped with a reflux condenser with a thermometer on a magnetic stirring bar in a water bath. Anhydrous sodium carbonate (1.0g, 0.1ml) was added to the mixture followed by the additions of DMF (5ml) to dissolve the compounds. The mixture was then heated with constant stirring for 30 mins at 70 -75 ^{0}C. After that 7-chloro-5,8-quinolinquinone (0.8g, 0.4mole) was then added to the mixture with continued starring at 70 – 75^{0}C for 6 h.

Dark reddish brown solid, yield: 75%. UV-VIS (ethanol) λmax (log ε): 203 (2.46); 264 (2.59); 341 (2.60); 437 (2.66) nm. IR (nujol) μmax: 3403cm^{-1}(N-H stretching), 1656cm^{-1} (C=O), 2926m^{-1} (C-H stretch for aromatics), 1446cm^{-1} (C=C and C= N stretch of aromatics) and 1287-1041cm^{-1} (C=C, and Ar–H bending). ^{1}H-NMR ($DMSO_{-d6}$) δ: 9.2 (s, 1H, C_2 proton), 8.6 (s, 1H, C_4 proton), 7.8 (d, 2H, C_3 and C_5 protons), 3.4 (s, 2H, NH_2). ^{13}C-NMR ($DMSO_{-d6}$) ppm: 125(C-C), 132-133(>C=C<), 147(>C=N), 173(>C=O, C-S).
The elemental analysis shows; Anal.calcd for $C_{13}H_7N_5S$ (%): C= 55.52; H = 2.49; N = 24.9; S = 11.38. Found C = 55.60; H = 2.50; N = 25.00; S =11.30.

3.3 General Procedure for the Copper Catalysed *N*-Arylation of Angular Triazaphenothiazinone.

A mixture of potassium phenyltriolborate 0.5g (1.5mmoles), $Cu(OAc)_2$ 0.6g (0.1mmole), trimetylamine-N-oxide 0.6g (1.1mmoles) and powdered 4A-molecular sieve(1g) in toluene(8ml) was stirred for 5 mins at room temperature. Then 1g (1.0mmole) of the triazaphenothiazinone was added and the mixture stirred for 20 hrs at room temperature. The product was then purified by chromatography on silicagel

3.3.1 11–(Phenylamino)–1, 8, 10-Triazabenzo [a] Phenothiazin–5-one

Dark red solid. yield: 70%. UV-VIS (ethanol) λmax (log ε): 226 (1.06); 274(1.02); 360 (1.14); 497 (1.07) nm. IR (nujol) μmax: 3432cm^{-1} (N-H stretch), 1653cm^{-1} (C=O stretch), 1584 and 1482cm^{-1} (C=N of pyrimidines), 1390cm^{-1} (C=CH and Ar-H stretch), and 1280-1037.cm^{-1} (C=CH and Ar-H stretching out plane vibration). ^{1}H-NMR ($DMSO_{-d6}$) δ: 9.2 (s, 1H, C_2 proton), 7.7 (d, 2H, C_3 and C_9 protons), 7.3 (s, 1H, C_6 proton), 6.7 (d, 2H, Ar-H), 3.4 (s, 1H, NH). ^{13}C-NMR ($DMSO_{-d6}$) ppm: 125(C-C), 132-133(>C=C<), 143(>C=N).
The elemental analysis shows; Anal.calcd for $C_{19}H_{11}N_5$ S (%): C= 63.86; H = 3.08; N = 19.61; S= 8.96. Found: C = 63.82; H = 3.10; N = 19.69; S = 9.00.

3.3.2 11 – (4-Bromophenylamino) 1, 8, 10-Triazabenzo [a] Phenothazin–5-One

Red solid. yield: 75%. UV-VIS (ethanol) λmax (log ε): 202 (2.22); 208 (1.75); 361 (1.79); 460 (2.03); 499 (2.01) nm. IR (nujol) μmax: 3358cm-^{1}(N-H stretching), 1656cm-^{1} (C=O stretching), 1493cm-^{1} (C=N stretching in pyrimidines), 1341cm-^{1} (C=C-H and Ar-H stretch) and 1274-1171cm^{-1} (C=CH and Ar-H bending out of plane).). ^{1}H-NMR ($DMSO_{-d6}$) δ: 9.7 (s, 1H, C_2 proton), 7.8 (d, 2H, C_3 and C_9 protons), 7.3 (s, 1H, C_6 proton), 6.7 (d, 2H, Ar-H), 3.4 (s, 1H, NH). ^{13}C-NMR ($DMSO_{-d6}$) ppm: 127 (C-C), 132-133 (>C=C<).
The elemental analysis shows; Anal.calcd for $C_{19}H_7N_5SBr$ (%): C = 52.29; H = 2.29; N = 16.00; Br = 18.35; S = 7.34. Found: C = 52.30; H= 2.29; N = 16.00; Br = 18.39, S =7.30.

3.3.3 11-(3-Nitrophenylamino)-1, 8, 10- Triazabenzo[a]Phenothiazin-5-one

Brownish red solid. yield: 65%. UV-VIS (ethanol) λmax (log ε): 202 (2.23); 208 (1.18); 363 (1.78); 460 (2.07)nm. IR (nujol) μmax: 3452cm-^{1} (N-H stretch), 1651cm-^{1} ((C= O), 1494cm-^{1} (C=N stretch), 1391cm-^{1}(C=CH and Ar-H stretch) and 1275 -1174.69 cm-^{1} (C=CH and Ar-H vibration out of plane).

4.0 Conclusion

Copper catalysed *N*-arylation is an efficient route to synthetic organic coupling reaction.

References

Zhoa,C.G., Hu,J ., Zhang,Y.L., Zhang,J . (2001): Synthesis, Characterization of 4{[C7-chloro-2-nitrophenothiazin-10-phenyl-methyl]-amino}-benzoic acid derivatives, *J. Chem. Pham. Res*., **3(1)**, 564.
Kalkanidiz, E.N., Tilley, N., and Deady,L.W. (2002) : phenothiazine antimalarial; its Synthesis and antimalarial activities , *Biochem. Pharmacol*: **63**(5), 833.
Mretzsch,F.(1954), *Angew. Chem*., **66**, 363. (b) Bodea,C.Y., and Silberg, I. A. (1968), *Heterocyclic. Chem*, **9**,321.
Okafor, C.O., Okerelu, I.O., and Okeke, S.I., (1986): *Vat dyes from three new Heterocyclic rings in dyes and pigments*, **8**,p.11-24.
Franz, A.W., Zhou,Z., Turdeon,R., Wagerer,A., Sarkar, B., Hartmoan, M., Emst, S., Thel,W. R., and Multer, T.J.J. (2009), *Eur. J. org. Chem*., 3895. (b) Barkscrat, C.S., Stoycheva, S., Himmelhaus, M. and Muller, T.J.J., (2010), *chem. matter*., **22,** 52.
Nakadan, N., Imabayashi, S. and Watanabe, M., (2005), *Longmuir Chem. Eur. J*.**, 22**,1871.
*Rang-Dale et al.,pharmacology, 6th edition.
Okafor, C.O. (1971) *Int. J. Sulfur Chem*. **6B**, 237.
Okafor, C.O. (1978), *phosphorus and sulphur*, **4,** 79
Okafor, C.O., (1986); The chemistry and Application of angular phenothiazine. *Dyes and Pyments*: **7**(4) 281-287.

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