Asian Journal of Chemistry; Vol. 30, No. 10 (2018), 2317-2321

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2018.21477

Synthesis of Functionalized Triphenodioxazines *via* Palladium Catalyzed Cross-Coupling Reactions

U.C. OKORO[1], M.A. EZEOKONKWO[1,*], A. UTIME[1], E.U. GODWIN-NWAKWASI[2], F.N. IBEANU[3] and S.N. OKAFOR[4]

[1]Department of Pure and Industrial Chemistry, Faculty of Physical Sciences, University of Nigeria, Nsukka 410001, Enugu State, Nigeria
[2]Department of Chemistry, College of Natural & Applied Sciences, Gregor University, Uturu, Abia State, Nigeria
[3]School of General Studies, Natural Science Unit, University of Nigeria, Nsukka 410001, Enugu State, Nigeria
[4]Department of Pharmaceutical and Medicinal Chemistry, University of Nigeria, Nsukka 410001, Enugu State, Nigeria

*Corresponding author: E-mail: mercy.ezeokonkwo@unn.edu.ng; mercy.ezeokonkwo@yahoo.com

Received: 25 May 2018; *Accepted*: 19 July 2018; *Published online*: 31 August 2018; AJC-19065

In this study, palladium catalyzed cross coupling reaction for the arylation of linear diaza triphenodioxazine is reported. The reaction of 2,5-dibromo-1,4-quinone with two molar equivalents of 2-amino-3-hydroxypyridine in anhydrous basic medium furnished 1,8-diazatriphenodioxazine (**9**) in good yield. The non aza analogue and parent ring of this ring system was also obtained under similar conditions. 6-Bromo-1,8-diazatriphenodioxazine (**10**) was formed by bromination of compound **9** in glacial acetic acid. Functionalized aryl derivatives of **9** were obtained by cross coupling reactions between substituted boronic acids and **10** under the catalytic influence of Pd[dppb]Cl_2/1,4-*bis*(2-hydroxy-3,5-di-*tert*-butylbenzyl)piperazine system.

Keywords: Triphenodioxazines, Palladium cross-coupling reactions, Aza analogue, Suzuki-Miyaura reactions, Boronic acids.

INTRODUCTION

The synthesis of phenoxazine derivatives and the isolation of natural phenoxazinones [1] have been a subject of continuing interest over the years due to the wide range of applications of these compounds. Notable among the natural products derived from phenoxazine ring skeleton are actinomycin [2] antibiotics isolated from *streptomyces* organisms, ommatin D [3], the red-brown pigment isolated from small tortoise-shell butterfly, *Vanessa aurticae*, the questiomycines [4-6] from *Waksmania aerate* and *Pseudomonas iodinum* and the cinnabarins [7,8] from wood-rotting fungi, *Coriolus sanquineus* and *Trametes cinabarina*. Apart from questiomycin and actinomycin antibiotics, which are notable for their antituberculosis and antitumor action, respectively. Most known phenoxazinones are pigments in their natural sources although some of them have been synthetically modified to be applicable as dyes [9-11].

In view of the reports [12-18] on the pharmacological activities of phenothiazines and phenoxazines, attention was shifted from their dyeing properties to a study of their biological activities. Phenothiazines and phenoxazines ring systems are vital component of various drugs used as antitumor agents, seductive, anticancer, antituberculosis, tranquilizers, bactericides, antiepilectics and parasiticides [19-22]. Recently a water soluble 2-amino-4,4′,7-dimethyl-3*H*-phenoxazine was reported to possess antiproliferative, immunosuppressive, antibacterial, antiviral effects [23]. Apart from their pharmacological properties, phenoxazines also find applications in material sciences such as laser dyes [24], electromagnetic materials [25], organic lights [26], thin film transistors [27], solar cells [28-31] and optical recording materials [32].

Although Agarwal and Schaffer [33] reported the synthesis of triphenodioxazine (**5**) as a byproduct among others following the report of Musso and Beecken [34] under the conditions of angular phenoxazine synthesis, there has been practically no report of any synthesis directed to the formation of **5** as the target compound. Again, our group is unaware of any report of aza analogue of this ring system in spite of the usual known superiority of azaphenoxazines and phenothiazines [35] over their carbocyclic counterparts. We are now reporting the synthesis of diaza-analogue of triphenodioxazine and this is one out of the 22 possible diaza analogues of this ring system. In our ongoing medicinal chemistry program we required the synthesis of 6-substituted derivatives of aza analogue of

triphenodioxazine for biological activities and for structure activity relationship studies. The application of modern synthetic approaches of the Suzuki-Miyaura type cross coupling reactions would offer elegant and straight-forward route to arylated triphenodioxazine *via* a halogenated triphenodioxazine. Although significant advances have occurred in the metal-catalyzed [36] cross coupling reactions involving halogeno arenes in the recent time, application of this coupling to various heterocyclic structures is still a relatively unexplored process [37,38]. Again, among the various methods known to biaryl synthesis, Suzuki-Miyaura cross coupling is a powerful method for the formation of C(sp^2)-C(sp^2) bonds under mild conditions [39] and the application of this methodology to various heterocyclic systems still remains unabated.

As part of our interest in the synthesis of new heterocyclic compounds and their derivatives [40,41], we report herein the synthesis of a new diaza analogue of triphenodioxazine and its aryl derivatives of pharmaceutical interest.

EXPERIMENTAL

Melting points were determined on Fisher-Johns apparatus and are uncorrected. Ultraviolet and visible spectra were recorded on Scan Buffer 16 Cecil 9050 spectrophotometer. The absorption maxima are given in nanometers. Infrared spectra were recorded on NICOLET AVATAR 330 FT-IR spectrophotometer using KBr (unless otherwise stated) and absorptions are given in wavenumbers. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian NMR-Mercury 200BB spectrometer operating at 200 and 50 MHz, respectively. Chemical shifts are in ppm using tetramethylsilane as internal standard. Gas chromatographic analysis was obtained on a Perkin- Elmer Clarus 500 GC/ Hewlett Packard G 1800 GCD system equipped with a parcked column. Mass spectra were recorded on a Shimadzu LKB- 9000 spectrometer. Elemental analysis was performed on a Perkin-Elmer 240 analyzer. All solvents were of technical grade and were purchased from Zayo-Sigma (local vendor). 2,5-Dibromo-1,4-quinone (**6**) [42] and 1,4-*bis*(2-hydroxy-3,5-di-*t*-butyl)-piperazine (**14**) [43] were synthesized as described. 2-Amino-3-hydroxypyridine (**8**), 2-aminophenol (**7**) and all palladium source catalysts were purchased from Aldrich.

Synthetic details for triphenodioxazine (5) and diaza analogue (9): Aminophenol (23 mmol) was mixed with anhydrous sodium acetate (24 mmol) and charged into a two-necked round bottomed flask fitted with reflux condenser. A mixture of benzene (40 mL) and DMF (2 mL) was added. The resulting mixture was heated under reflux for 45 min. A suspension of 2,5-dibromo-1,4-quinone (11 mmol) in benzene (20 mL) was added and the resulting mixture heated at 80 ºC for 4 h. At the end of the refluxing period, benzene was removed by vaccum distillation while the residue mixed with cold water and stirred. The resulting solid was collected by filtration and re-crystallized from aqueous DMF. Analytical samples were obtained by column chromatography on silica gel (type 60) and using dichloromethane (DCM) as eluting solvent.

General procedure for Pd-catalyzed coupling of compound 10 with substituted boronic acids: In a 50 mL two-necked round-bottomed flask, palladium-precausor (0.5 mol %), ligand (0.5 mol %) toluene (5 mL) and DMF (1 mL) were placed. The mixture was flushed with nitrogen with stirring for 10 min. [except for $Pd(COD)Cl_2$] where reactions were carried out under aerobic conditions). After this 6-bromo-1,8-diazatriphenodioxazine (**10**) (0.5 mmol); aryl boronic acid (0.85 mmol) and base (1 mmol) were added and the reaction mixture heated under reflux and under nitrogen atmosphere [except for $Pd(COD)Cl_2$] for the specified reaction time. At the end of heating period the reaction mixture was cooled to room temperature and striped of solvent under reduced pressure.

The residue was diluted with water (10 mL) and DCM (8 mL). This was followed by extraction, three times (3 × 5 mL) with DCM. The combined extract was dried with $MgSO_4$ and striped of solvent under reduced pressure. The crude product was subjected to column chromatography on silica gel (type 60) using DCM-hexane (10:1) as the eluting solvent mixture. The GC-MS analysis was done by re-dissolving the residue in DCM (6 mL) and using syringe to draw aliquot from this solution for each run.

Triphenodioxazine (5): Orange-brown powder, m.p. > 300 ºC, Yield: 82 %. UV-visble (DMF) λ_{max} (log ε): 271 (4.063), 422 (4.004) nm. NMR (acetone-d_6) δ_H: 7.08 (s, 2H); 7.60 (dd, 2H, *J* = 7.0 Hz); 7.26 (dd, 2H, *J* = 5.0 Hz); 6.78 (q, 2H, *J* = 5.0 Hz); 6.44 (q, 2H, *J* = 7.0 Hz); δ_C: 38.97, 39.36,8, 39.79, 40.21, 40.63, 41.04, 99.06, 104.13, 116.64, 125.99, 128.68, 129.52, 134.42, 142.63, 148.07, 148.95, 149.58. MS, *m/z* : 286 (M^+). Anal. Calcd. for $C_{18}H_{10}N_2O_2$ (%): C,75.52; H, 3.50; N, 9.79. Found: C, 75.40; N, 3.52; N, 9.60.

1,8-Diazatriphenodioxazine (9): Greenish-grey powder, m.p. > 300 ºC, Yield: 70 %. UV-visble (DMF) λ_{max} (log ε): 202 (3.271); 404 (4.012); 880 (3.610) nm. NMR (acetone-d_6) δ_H: 7.26 (s, 2H); 7.65 (dd, 2H, *J* = 8.0 Hz); 7.00 (dd, 2H, *J* = 5.0 Hz); 6.20 (q, 2H, *J* = 9.5 Hz); δ_C: 99.5, 103.8, 107.6, 109.8, 116.3, 119.6, 120.2, 124.2, 126.0, 142.8, 147.9. MS; m/z : 288 (M^+). Anal. Calcd. for $C_{16}H_8N_4O_2$ (%): C, 66.67; H, 2.80; N, 19.44. Found: C, 66.69; H, 2.76; N, 19.33.

6-Bromo-1,8-diazatriphenodioxazine (10): This compound was obtained following literature procedure [42]. Grey powder, m.p. > 270 ºC, Yield: 60 %. UV-visble (DMF) λ_{max} (log ε): 202 (4.810); 204 (3.723); 800 (4.400) nm. MS; *m/z*: 367 (M^+), 369 ($M^+ + 2$). Anal. Calcd. for $C_{16}H_7N_4O_2Br$ (%): C, 52.32; H, 1.91; N, 15.26; Br, 21.80. Found: C, 52.22; H, 2.00; N, 15.30; Br, 21.90.

6-Phenyl-1,8-diazatriphenodioxazine (11a): Orange-red oil, Yield: 95 %. UV-visble (DMF) λ_{max} (log ε): 206 (4.801), 500 (4.389) nm. ^{1}H NMR (DMSO-d_6) δ: 8.80 (dd, 2H, *J* = 8.60 Hz), 7.80 (dd, 2H, *J* = 6.0 Hz), 7.40 (dd, 2H, *J* = 9.2 Hz), 7.00 (m, 5H, arom.). MS, *m/z*: 364 (M^+). Anal. Calcd. for $C_{22}H_{12}N_4O_2$ (%): C, 72.53; H, 3.30; N, 15.38. Found: C, 72.60; H, 3.42; N, 15.40.

6-(3-Chlorophenyl)-1,8-diazatriphenodioxazine (11b): Red oil, Yield: 90 %. UV-visble (DMF) λ_{max} (log ε): 204 (3.608), 502 (4.718) nm. ^{1}H NMR (DMSO-d_6) δ: 9.02 (dd, 2H, *J* = 8.40 Hz), 8.04 (dd, 2H, *J* = 5.80 Hz), 7.60 (d, 2H, *J* = 9.0 Hz), 7.20 (m, 4H, arom.), 6.80 (s, 1H, olefinic). MS, *m/z*: 398 (M^+), 400 ($M^+ + 2$). Anal. Calcd for $C_{22}H_{11}N_4O_2Cl$ (%): C, 66.25; H, 2.76; N, 14.05; Cl, 8.91. Found: C, 66.20, H, 2.69; N, 14.00; Cl, 8.92.

6-(3-Bromophenyl)-1,8-diazatriphenodioxazine (11c): Purplish-red oil, Yield: 92 %. UV-visble (DMF) λ_{max} (log ε):

204 (3.340), 560 (4.458) nm. ^{1}H NMR (DMSO-d_6) δ: 8.90 (dd, 2H, *J* = 8.80), 8.20 (dd, 2H, *J* = 6.20 Hz), 7.80 (dd, 2H, *J* = 8.60 Hz), 7.40 (m, 4H, arom.), 6.60 (s, 1H, olef.). MS, *m/z*: 443 (M^+), 445(M^+ + 2). Anal. Calcd for $C_{22}H_{11}N_4O_2Br$ (%): C, 59.59; H,2.48; N,12.64; Br, 18.06. Found: C, 59.60; H, 2.35; N, 12.70; Br, 18.1.

6-(3-Nitrophenyl)-1,8-diazatriphenodioxazine (11d): Orange-red oil, Yield: 82 %. UV-visble (DMF) λ_{max} (log ε): 301 (4.659), 540(3.285) nm. IR (nujol) λ_{max}: 1559 (NO_2) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ: 9.02 (dd, 2H, *J* = 9.0Hz), 8.60 (dd, 2H, *J* = 6.20 Hz), 8.00 (dd, 2H, *J* = 8.9 Hz), 7.60 (m, 4H, arom.), 6.80 (s, 1H, olef.). MS, *m/z*: 409 (M+). Anal. Calcd for $C_{22}H_{11}N_5O_4$ (%): C, 64.55; H, 2.69; N, 17.11. Found: C, 64.60; H, 2.62; N, 17.21.

6-(4-Nitrophenyl)-1,8-diazatriphenodioxazine (12e): Red oil, Yield: 96 %. UV-visble (DMF) λ_{max} (log ε): 300 (4.753), 556 (3.946) nm. IR (nujol) λ_{max}: 1560 (NO_2) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ: 9.60 (dd, 2H, *J* = 8.80 Hz), 8.90 (dd, 2H, *J* = 5.80 Hz), 8.20 (dd, 2H, *J* = 9.0 Hz), 7.80 (m, 4H, arom.), 7.00 (s, 1H, olef.). MS, *m/z*: 409 (M^+). Anal. Calcd for $C_{22}H_{11}N_5O_2$ (%): C, 64.55; H, 2.69; N, 17.11. Found: C, 64.58; H, 2.70; N, 17.19.

RESULTS AND DISCUSSION

The reaction of 2,5-dibromo-1,4-quinone (**6**) with two molar equivalents of 2-aminophenol (**7**) under anhydrous basic medium gave triphenodioxazine (**5**) in 72 % yield. Microanalysis and mass spectroscopy were consistent with the molecular formula $C_{18}H_{10}N_2O_2$. Confirmatory evidence of structure is provided by ^{1}H NMR spectrum. Although the spectrum is more complicated than the usual ABX systems, the splitting pattern for protons resembles a case of anticipated ABXY system with respect to aromatic protons. Five distinct absorption signals are indicated. A two proton (2H) singlet centered at 7.08 ppm has been attributed to the two equivalent protons located at C-6 and C-13. These protons are olefinic, whose position of absorption has been shifted downfield due to the electron withdrawing effect of nitrogen and oxygen heteroatoms. The protons at positions 1,2,3 and 4 are chemically equivalent to those at positions 8,9,10 and 11, respectively. Therefore signals at 7.60 ppm were attributed to C-4 and C-11 protons which appear as doublets of doublets (quartets) *J* = 7.0 Hz due to spin-spin splitting arising from the influence of C-2 and C-3 protons in a typical ABX system. By similar reasoning the quartet signals at 7.26, 6.78 and 6.44 ppm have been attributed to protons at C-1 & C-8; C-3 & C-10; C-2 & C-9, respectively.

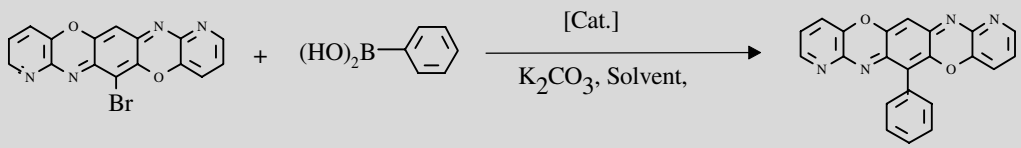
In a similar development the reaction of **6** with two molar equivalents of 2-amino-3-hydroxypyridine (**8**) gave 1,8-diazatriphenodioxazine (**9**) in 70 % yield. Microanalysis and mass spectroscopy agreed with the molecular formula $C_{16}H_8N_4O_2$. Confirmatory evidence of structure was provided by the proton NMR spectrum which gave a singlet signal at δ 7.26 (6-H & 13-H), 7.65 (q, *J* = 8.0 Hz, 2-H & 9-H), 7.00 (q, *J* = 5 Hz, 4-H &11-H); 6.20 (q, *J* = 9.5 Hz, 3-H & 10-H).

Bromination of diazatriphenodioxazine (**9**) in glacial acetic acid afforded 6-bromo-1,8-diazatriphenodioxazine (**10**) in 80 % yield contrary to our expectation of 6,13-dibromo derivative which was formed in less than 10 % yield. The authenticity of **10** was established by elemental analysis and spectroscopy. In arylation of 6-bromo-1,8-diazatriphenodioxazine (**10**) Suzuki-Miyaura (SM) cross-coupling methodology was employed. Initially, we started by investigating the influence of solvent in the coupling reactions in order to optimize the reaction conditions.

In this direction, a number of solvents (both polar and non-polar) including solvent mixtures were tried. A model reaction was carried out using compound **10** and phenylboronic acid at reflux temperature of most solvents (except otherwise stated) and Pd(COD)Cl_2/1,4-*bis*(2-hydroxy-3,5-di-*tert*-butyl)piperazine (**12**) in the ratio of 1:1 as catalyst system (Table-1). Of all the solvents investigated, only a mixture of DMF/toluene (1:5) gave quantitative results (entry 6, Table-1). Its not surprising however, as this solvent system gave the best solubility of **10** at reflux temperature of toluene. The optimization experiment was further extended to different bases (Table-2). In this case, K_2CO_3, K_3PO_4 and Na_2CO_3 proved superior to other bases investigated. Under the optimized conditions, a number of substituted arylboronic acids were employed in the coupling reactions (Table-3). In all cases, high yields of expected products were observed. When the reactions were tried at room temperature, no significant reaction occurred as most starting materials were recovered.

To investigate the catalytic value of various palladium sources in the presence of non-phosphorus ligand **12**, coupling reactions between 6-bromo-1,8-diazatriphenodioxazine (**10**) and phenylboronic acid were carried out in DMF/toluene using different palladium systems at 70 ºC for 50 min with minimum catalytic loading. The results are shown in Table-4. Interestingly, Pd(dppb)-Cl_2/L gave the highest conversion (66.02 %) and TON of 132,040.

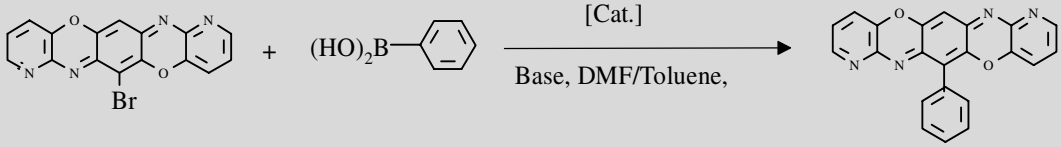
TABLE-1
SCREENING OF SOLVENTS FOR THE EFFECT OF SOLVENT ON SUZUKI-MIYAURA COUPLING REACTION[a]



Entry	Solvent	Conversion[b]	Entry	Solvent	Conversion[b]
1	Toluene[c]	65	5	Dioxane[e]	58
2	Methanol[c]	50	6	DMF/Toluene[c]	98
3	Acetone[c]	55	8	DMSO[e]	60
4	DMF[d]	68			

[a]Reactions of **10** (0.5 mmol), phenylboronic acid (0. 85 mmol), K_2CO_3 (1 mmol), catalyst (0.5 mol %), solvent (5 mL); [b]Conversion to the coupled product based on the remaining 10 was determined by GC; [c]Under reflux condition; [d]Reaction carried out at 70 °C; [e]Reaction carried out at 100 °C

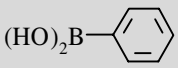
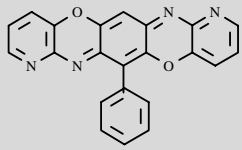
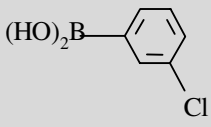
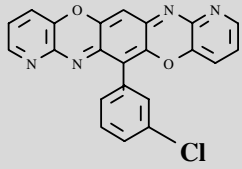
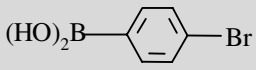
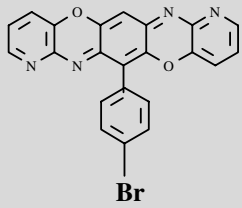
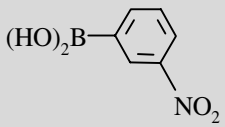
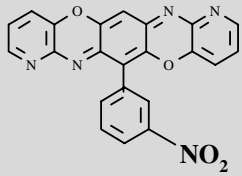
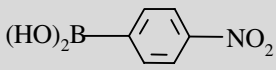
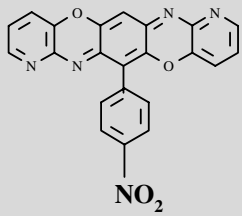
TABLE-2
SCREENING OF BASES FOR SM COUPLING REACTION[a]



Entry	Base	Conversion[b]	Entry	Base	Conversion[b]
1	K_3PO_4	100	4	Et_3N	90
2	K_2CO_3	100	5	Cs_2CO_3	90
3	Na_2CO_3	100	6	LiOH	80

[a]Reactions of **10** (0.5 mmol), phenylboronic acid (0. 85 mmol), K_2CO_3 (1 mmol), catalyst (0.5 mol %), solvent (5 mL); [b]Conversion to the coupled product based on the remaining **10** was determined by GC.

TABLE-3
Pd-CATALYZED ARYLATION OF AZATRIPHENODIOXAZINE[a]

Entry	Boronic acid	Product	Time	Yield[b] (%)
1			10 h	95
2			15 h	90
3			15 h	92
4			20 h	82
5			20 h	96

[a]Reaction of **10** (0.5 mmol), arylboronic acid (0.85 mmol), K_3PO_4 (1 mmol), DMF (1 mL), Toluene (5 mL) and catalyst (0.5 mol %); [b]Isolated yield.

This was followed closely by Pd(COD)Cl_2/L with 62.08 % conversion and TON of 124,160. Pd(dppe)Cl_2/L gave a conversion of 60.90 % with a TON of 121,800. When Pd(dppb)Cl_2 was used in the absence of ligand **12**, the conversion diminished to 10.84 % only with a TON of 21,680. This shows that ligand was necessary for good catalytic activity. This is consistent with earlier observation in the literature [44]. It should be noted that while the reactions with Pd(dppb)Cl_2/L or Pd(dppe)Cl_2/L were carried out under nitrogen atmosphere, the reaction using Pd(COD)Cl_2/L was carried out under aerobic condition.

Conclusion

The synthesis of first diaza analogue of triphenodioxazine has been accomplished. Functional derivatives of this ring system have been prepared by palladium catalyzed cross coupling. Typical reactions of the Suzuki-Miyaura reactions giving rise

TABLE-4
COMPARISON OF VARIOUS Pd(II) SYSTEMS[a] AND EFFECT OF LOW CATALYST LOADING

Entry	Catalyst	Conversion[b] (%)	TON
1	$Pd(COD)Cl_2/L^c$	62.08	124,160
2	$Pd(dppb)Cl_2/L^d$	66.02	132,040
3	$Pd(dppe)Cl_2/L^d$	60.90	121,800
4	$Pd(COD)Cl_2$ [c]	10.50	21,000
5	$Pd(dppb)Cl_2$ [d]	10.84	21,680

[a]Reaction of **10** (0.5 mmol), phenylboronic acid (0.85 mmol), catalyst (0.0005 mmol %), time (50 min), K_3PO_4 (1 mmol), DMF (1 mL), toluene (5 mL); [b]Conversion to the coupled product was based on the remaining 10 and was determined by GC; [c]Reaction carried out under aerobic condition at 70 °C; [d]Reaction carried out under nitrogen atmosphere at 70 °C.

to arylated systems. Further work on the investigation of biological activities of these compounds will be carried out in our laboratory. The next frontier is the conversion of halogenated aryl derivatives to wire-like oligotriphenodioxazines.

ACKNOWLEDGEMENTS

Grant No. 94/106 from the Senate Research Grants Committee of the University of Nigeria supported this work. The authors are grateful to Dr. A. Ahman formally of the Central Science Laboratory, University of Cairo, Egypt for part of microanalysis and to Dr. C. Okereke of University of Oxford, UK for mass spectra. The technical assistance of Messrs A. E. Umo, J.P. Ugwu, E.C. Mbaoji and J.I. Ugwu are deeply appreciated.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. M. Ionescu and H. Mantsch, Advances in Heterocyclic Chemistry, Katritzky A R. and Bouton A. J.; Eds, Academic Press Inc.: New York, N.Y., 8, p. 83-113, (1967).
2. H. Brockman, The Chemistry of Natural Products, International Union of Pure and Applied Chemistry Section of Organic Chemistry, Burterworths Purblishers and Co. Ltd.: London, p. 405-424, (1961).
3. A. Butenandt and N. Biekert, *Hoppe Seylers Z. Physiol. Chem.*, **258**, 321 (1960).
4. P.M. Nair and C.S. Vaidyanathan, *Biochem. Biophys. Acta*, **81**, 507 (1964); *Chem. Abstr.*, **60**, 12292H (1964).
5. M.J. Matsuoka, *Antibiotics (Tokyo) Ser. A.*, **13**, 121 (1960), *Chem. Abstr.*, **56**, 9365e (1962).
6. K. Azani, K. Isono, K. Okuma and S. Suzuki, *Rika Gaku Kenkyusho Hokoku*, **36**, 577 (1960), *Chem. Abstr.*, **55**, 25150f (1961).
7. K. Lemberg, *Aust. J. Exp. Biol. Med. Sci.*, **30**, 271 (1952); https://doi.org/10.1038/icb.1952.24.
8. G.W.K. Cavill, P.S. Clezy, J.R. Tetaz and R.L. Werner, *Tetrahedron*, **5**, 275 (1959); https://doi.org/10.1016/0040-4020(59)80019-3.
9. C.O. Okafor, *Dyes Pigments*, **7**, 103 (1986); https://doi.org/10.1016/0143-7208(86)85003-3.
10. C.O. Okafor, *Tetrahedron*, **44**, 1187 (1988); https://doi.org/10.1016/S0040-4020(01)85898-1.
11. U.C. Okoro and C.O. Okafor, *J. Nig Acad. Sci.*, **2**, 77 (1990).
12. S.P. Massie, *Chem. Rev.*, **54**, 797 (1954); https://doi.org/10.1021/cr60171a003.
13. C. Bodea and I. Silberg, *Advances in Heterocyclic Chemistry*, A.R. Katritzky and A J. Boulton, Eds, Academic Press Inc.: New York, N. Y, 9, p.231, (1968).
14. E. Von Schenker and H. Herbst, Progress in Drug Research, E. Jucker, Ed., Birkhauser Verlag: Basel, 9, p.269-627, (1963).
15. M.A. Ezeokonkwo, F.O. Ugwuona and I.C. Ugwu, *Asian J. Chem.*, **27**, 3843 (2015); https://doi.org/10.14233/ajchem.2015.19012.
16. D.I, Ugwu, U.C. Okoro and T.D. Chukwurah, *Med. Chem.*, **4**, 357 (2014).
17. E.A. Onoabedje, U.C. Okoro, D.W. Knight and A. Sarkar, *J. Heterocycl. Chem.*, **53**, 1787 (2016); https://doi.org/10.1002/jhet.2485.
18. F.N. Ibeanu, E. A. Onoabedje, A. Ibezim and U.C. Okoro, *Med Chem Res.*, (2018),
19. C.S. Kramer, T. J. Zimmermann, M. Sailer and T.J. Muller, *Synthesis*, **9**, 1163 (2002).
20. O. Wesolowska, J. Molnar, G. Westman, K. Samuelsson, M. Kawase, L. Ocsovszki, N. Motohashi and K. Michalak, **20**, 109 (2006).
21. T. Shimamoto, A. Tomada, R. Ishida and K. Ohyashiki, *Ame-Asso. for Cancer Res.*, **7**, 704 (2001).
22. E.U. Godwin-Nwakwasi1, U.C Okoro, M.A. Ezeokonkwo, F.N. Ibeanu and I.C. Ugwu, *Org. Med. Chem. Int. J.*, **5**, (2018).
23. E.A. Onoabedje, U. C. Okoro, A. Sarkar and D.W. Knight, *J. Sulfur Chem.*, **37**, 269 (2016).
24. A. Nowakowska-Oleksy, J. So³oducho and J. Cabaj, *J. Fluorescence*, **21**, 169 (2011).
25. Y. Zhu, A. Babel and S.A. Jenekhe, *Macromolecules*, **38**, 7983 (2005); https://doi.org/10.1021/ma0510993.
26. K.K.K. Sharma, S.G. Swarts and W.A. Bernhard, *J. Phys. Chem.*, **115**, 4843 (2011); https://doi.org/10.1021/jp200902h.
27. A.P. Kulkarni, Y. Zhu, A. Babel, P.-T. Wu and S.A. Jenekhe, *Chem. Mater.*, **20**, 4212 (2008); https://doi.org/10.1021/cm7022136.
28. Z. Wan, C. Jia, Y. Duan, L. Zhou, Y. Lin and Y. Shi, *J. Mater. Chem.*, **22**, 25140 (2012); https://doi.org/10.1039/c2jm34682f.
29. A.S. Hart, C.K.C. Bikram, N.K. Subbaiya, P.A. Kar and F. D'Souza, *Appl. Mater. Interfaces*, **4**, 5813 (2012); https://doi.org/10.1021/am3014407.
30. Z. Iqbal, W.Q. Wu, Z.S. Huang, L. Wang, D.B. Kuang, H. Meier and D. Cao, *Dyes Pigments*, **124**, 63 (2016); https://doi.org/10.1016/j.dyepig.2015.09.001.
31. H. Meier, Z.S. Huang and D. Cao, *J. Mater. Chem.*, **5**, 9828 (2017).
32. C.P. Constantin and M.D. Damaceanu, *J. Phys. Chem.*, **121**, 6300 (2017).
33. N.L. Agarwal and W. Schaefer, *J. Org. Chem.*, **45**, 2155 (1980); https://doi.org/10.1021/jo01299a024.
34. H. Musso and H. Beecken, *Chem. Ber.*, **94**, 585 (1961); https://doi.org/10.1002/cber.19610940305.
35. A. Von Schlichtegrol, *Arzneium-Forsch*, **7**, 237 (1957); *Chem. Abstr.*, **51**, 12349d (1957).
36. J.F. Hartwig, Handbook of Organopalladium Chemistry for Organopalladium Chemistry of Organic Synthesis, Wiley- Interscience: New York, NY, (2002).
37. Z.H. Peng, M. Journet and G. Humphrey, *Org. Lett.*, **8**, 395 (2006); https://doi.org/10.1021/ol052578p.
38. C. Enguehard-Gueiffier, I. Thery, A. Gueiffier and S.L. Buchwald, *Tetrahedron*, **62**, 6042 (2006); https://doi.org/10.1016/j.tet.2006.04.007.
39. (a) N. Miyaura and A. Suzuki, *Chem. Rev.*, **95**, 2457 (1995); https://doi.org/10.1021/cr00039a007.
(b) S.P. Stanforth, *Tetrahedron*, **54**, 263 (1998); https://doi.org/10.1016/S0040-4020(97)10233-2.
(c) A. Suzuki, *In Metal Catalyzed Cross-coupling Reactions;* F. Diederich, P.J. Stang, Eds.; Wiley-VCH: Weinheim, p.49-97, (1998).
40. U.C. Okoro, F. Okpunor and R.O. Ugwoke, *Int. J. Chem.*, **19**, 107 (2009).
41. U.C. Okoro, E. Onoabedje and E.M. Odin, *Int. J. Chem.*, **19**, 197 (2009).
42. T.J. Colacot, H. Qian, R. Cea-Olivares and S. Hernandez-Ortega, *J. Organomet. Chem.*, **637-639**, 691 (2001); https://doi.org/10.1016/S0022-328X(01)00981-0.
43. T.S. Wheeler, *Org. Synth. Coll.*, **4**, 478 (1963).
44. S. Mohanty, D. Suresh, M.S. Balakrishna and J.T. Mague, *Tetrahedron*, **64**, 240 (2008); https://doi.org/10.1016/j.tet.2007.10.081.