

## Research Article

# Design and Synthesis of Novel Gly-Tyro based Arylsulphonamoyl compounds as Anti-alzheimer's and Antioxidant Agents

Ike Ozoemena Christian <sup>1</sup>, Okoro Uchechukwu Christopher <sup>2</sup> and Ogbuanu Cyril Chinedu<sup>1</sup><sup>1</sup>Department of Industrial Chemistry, Enugu State University of Science and Technology, Enugu State, Nigeria.<sup>2</sup>Department of Pure and Industrial Chemistry, University of Nigeria Nsukka, Enugu State, Nigeria.

\*Corresponding author: E-mail: born2excell555@gmail.com


## Article Info

**Keywords:** Synthesis, Benzene-sulphonamide, Gly-Tyro Dipeptide, Anti-alzheimer's Activity, Antioxidant Activity.

Received: 20.04.2026;

Accepted: 11.06.2026;

Published: 20.06.2026

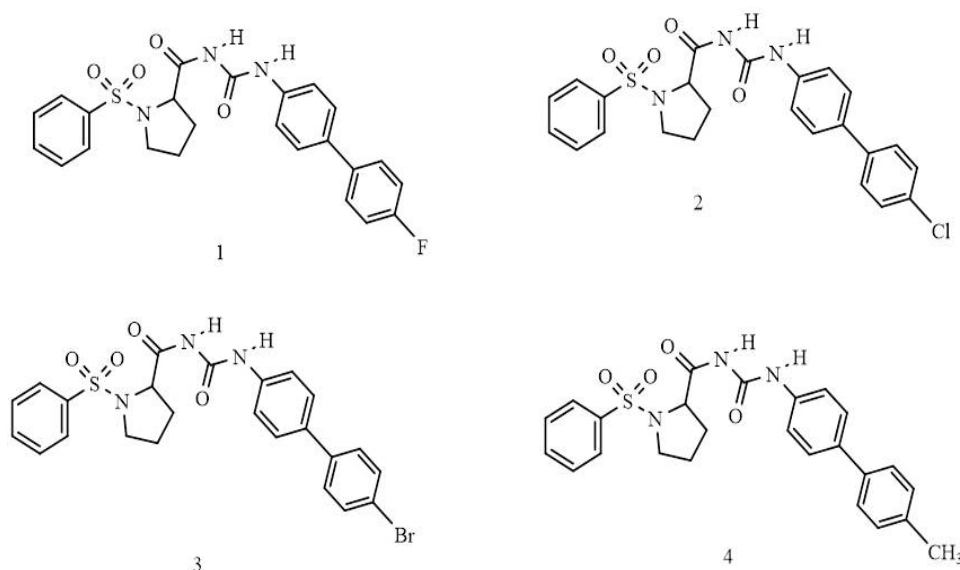
 © 2026 by the author's. The terms and conditions of the Creative Commons Attribution (CC BY) license apply to this open access article.

## Abstract

Four novel glycine-tyrosine dipeptide sulphonamide derivatives were synthesized, characterized via <sup>1</sup>HNMR, <sup>13</sup>CNMR, FTIR and HRMS spectroscopic techniques and their anti-alzheimer's, antioxidant activities were investigated. The base promoted reaction of substituted benzenesulphonyl chloride with L-glycine gave compound (7a-7b) in excellent yields. Compounds (12a-12d) were achieved by amidation of substituted benzene-sulphonamoyl derivatives with alkanamides (11) in the presence of EDC.HCl and HOBt as peptide coupling reagents. The antimicrobial properties were determined by agar dilution method and the antioxidant properties were also investigated. The anti-alzheimer's study revealed that the IC<sub>50</sub> value of compound 12c showed a significant inhibition of 0.65 mg/mL comparable with the IC<sub>50</sub> value of galantamine (0.70 mg/mL). In the antioxidant study, IC<sub>50</sub> value of compound 12b (0.76 mg/mL) is comparatively almost the same with that of vitamin C (0.79 mg/mL). This implies that compound 12b can be serve as a lead potent antioxidant agent.

## 1. Introduction

Sulphonamide conjugates has antimalarial properties that can alter the biosynthesis path way of folate responsible for the survival of the parasite [1, 2]. Sulfadiazine and dapson were amongst the first sulfa pharmacological agent to be used clinically for the treatment of malaria infections [1]. Dipeptides and peptides moieties are important structural motifs found in a broad range of clinically used drugs such as antimalarial, anti-inflammatory agents, anticancer agent, anti-HIV drugs and antiviral drugs [3–5]. Both naturally derived and synthetic dipeptides and peptides have been reported to show potent antimicrobial properties [6–9]. Alzheimer's disease is a major health issue for all communities. It is a neurodegenerative disease that causes mental conditions such as memory loss and cognitive impairment [10]. Alzheimer's disease affects 50 million people worldwide with 5.4 million of them being Americans. A new case of alzheimer's disease is anticipated to occur every 33 seconds by 2050 with an estimation of 11-16 million patients (Alzheimer's association, 2015). Attah *et al* [9], described the synthesis of Pro-Gly based dipeptide containing sulphonamide moieties. The authors treated proline with benzenesulphonyl chloride to afford (phenylsulphonyl)proline. The amidation reaction of (phenylsulfonyl)phenylalanine derivatives with deboc-aminated glycine derivatives gave the targeted compounds Figure 1. The Authors claimed that the compound exhibited excellent antioxidant.



**Figure 1:** Chemical structures of sulphonamide derivatives that exhibited antioxidant properties

## 2. Materials and methods

### 2.1. Materials

Reagents were purchased from Sigma Aldrich. Melting points of the novel compounds were carried out using John's melting point apparatus and are uncorrected. Infrared spectra data were measured on 8400s Fourier Transform Infrared (FTIR). Nuclear Magnetic Resonance ( $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$ ) analysis were done using NMR spectrophotometer and chemical shifts were measured in part per million with tetramethyl silane as reference point. All reactions were monitored by thin layer chromatography (TLC) on precoated silica gel 60 F 254 (mesh); spots were visualized under UV light. The anti-alzheimer's activity studies took place at the Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka while the antioxidant studies were carried out at the Biochemistry Department, University of Nigeria, Nsukka.

#### General procedure for the synthesis of Substituted Benzenesulphonamoyl derivatives (5a-5b)

Sodium carbonate ( $\text{Na}_2\text{CO}_3$ , 26.25 mmol) was weighed and added to a solution of L-glycine (12.5 mmol) in distilled water (50 mL) with continuous stirring using a magnetic stirrer until all the solute dissolved. The solution was cooled to  $-5^\circ\text{C}$  and appropriate substituted benzenesulphonylchloride (12 mmol) were added in four portions over a period of 1 h. The slurry was further stirred for 4 h at room temperature. The progress of the reaction was monitored using thin layer chromatography (TLC) (MeOH/DCM) 1:9). Upon completion, the mixture was acidified using 20% aqueous hydrochloric acid to pH of 2. The organic portion was extracted with dichloromethane ( $3 \times 50$  mL), brine ( $2 \times 50$  mL) and the crude products were obtained by suction filtration. The crude products were dried over fused silica gel in desiccators and recrystallized from methanol to give pure solid products.

#### General procedure of preparing boc-protected substituted alkanamide derivatives (10)

A mixture of *tert*-butoxycarbonyl tyrosine (16.90 mmol), 1-ethyl-3-(3-dimethyl aminopropyl carbodiimide hydrochloride (15.80 mmol) EDC, 1-hydroxybenzotriazole, HOBt, (12.90 mmol), triethylamine, TEA (20.0 mmol) and three different amines respectively in dichloromethane (40 ml) were added into a 100 mL round bottom reaction flask and stirred at room temperature for 17 h. The progress of the reaction was monitored using thin layer chromatography (TLC). At the end of reaction, the content of the flask was transferred into a separating funnel diluted with DCM (40 mL), washed with 1N HCl (50 mL), 5% sodium bicarbonate solution (50 mL) and brine (50 mL). The organic portion obtained was dried using anhydrous sodium sulphate and the solvent was removed under reduced pressure to give the crude products (11) which was then purified by column chromatography using silica gel [4]. The compounds were characterized.

#### General Procedure for the Synthesis of arylsulphonamoyl 'Gly-Tyr' Dipeptide Derivatives (12a -12d)

The carbamate derivatives (11) were stirred in 10% trifluoroacetic acid/ dichloromethane (TFA/DCM) to remove the *boc*-protecting group. After which the solvent was evaporated to obtain the substituted alkanamides in excellent yield. To a solution of appropriate substituted benzenesulphonamide (16.90 mmol), 1-ethyl-3-(3-dimethyl aminopropyl carbodiimide hydrochloride (15.80 mmol) EDCI, 1-hydroxybenzotriazole, HOBt, (12.90 mmol), triethylamine, TEA (20.0 mmol) and substituted protected alkanamide derivative (1.84 mmol) in dichloromethane (40 ml) was added into a 100 mL round bottom reaction flask and stirred at room temperature for 17 h. The reaction was monitored using TLC and at the end of reaction, the content of the flask was transferred into a separating funnel, diluted with DCM (40 mL), washed with 1N HCl (50 mL), 5% sodium bicarbonate solution (50 mL) and brine (50 mL). The organic portion obtained was dried using anhydrous sodium sulphate and the solvent was removed under reduced pressure to obtain the crude product which were then purified by column chromatography using silica gel and 3% methanol/dichloromethane to furnish (12a-12b) [4].

### Phenylsulphonyl)glycine (7a)

Yield 90.34%, mp, 157.9°C (lit m.p 160. 5°C). FTIR (KBr,  $\text{cm}^{-1}$ ): 3380 (OH), 3257 (NH), 3108 (C-Haromatics) 1744 (C=O), 1502, 1449 (C=C), 1349 ( $\text{SO}_2$ ).  $^1\text{H}$  NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 13.20 (s, 1H, OH of carboxylic acid), 7.92 (d, 1H,  $\text{SO}_2\text{-NH}$ ), 7.60 (d, 2H, Ar-H), 3.85 (s, 2H,  $\text{CH}_2$ ).  $^{13}\text{C}$ -NMR ( $\text{DMSO}_{d6}$ ) $\delta$ : 171.2 (C=O), 144.5 - 130.3 (aromatic carbons), 44.5 - 22.5 (aliphatic carbon). HRMS-ESI (m/z) for  $\text{C}_8\text{H}_9\text{NO}_4\text{S}$ : 215.0252 ( $\text{M}^+$ ), calculated, 215.0254.

### Tosylglycine (7b)

Yield 89.40%, mp, 138.8°C (lit m.p 140.5°C). FTIR (KBr,  $\text{cm}^{-1}$ ): 3287 (NH), 3108 (C-Haromatics), 2922 (C-H aliphatics), 1707 (C=O), 1535, 1431 (C=C), 1341 ( $-\text{SO}_2-$ ).  $^1\text{H}$  NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 13.10 (s, 1H, OH of carboxylic acid), 7.80 (d, 1H,  $\text{SO}_2\text{-NH}$ ), 7.70 (d, 2H, Ar-H), 3.86 (s, 2H,  $\text{CH}_2$ ), 2.4432 (s, 3H, Ar- $\text{CH}_3$ ).  $^{13}\text{C}$ -NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 172.64 (C=O), 137.46 - 106.31 (aromatic carbons), 44.54 - 22.56 (aliphatic carbon). HRMS-ESI (m/z) for  $\text{C}_9\text{H}_{11}\text{NO}_4\text{S}$ : 229.0407 ( $\text{M}^+$ ), calculated, 229.0408.

### 3-(4-Hydroxyphenyl)-2-((3-((4-methylphenyl)sulphonamido)-2-oxopropyl)amino)-N-phenylpropanamide (12a)

Yield 70%, Mp, 88°C. FTIR (KBr,  $\text{cm}^{-1}$ ): 3321 (NH), 3034 (C-H aromatics), 2928 (C-H aliphatic), 1670, 1650 (C=O of amide), 1436 (C=C aromatic), 1354, 1338 ( $-\text{SO}_2-$ ), 1174, 1084, (C-N).  $^1\text{H}$  NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 9.30 (s, 1H, Ar-OH), 8.32 (d, 2H, NH-amine), 7.85 (d, 1H,  $\text{SO}_2\text{-NH}$ ), 7.70 (dd, 4H, Ar-H), 4.20 (s, 1H,  $\text{CH}_2$ ), 2.48 (s, 3H, Ar- $\text{CH}_3$ ).  $^{13}\text{C}$ -NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 172.61 and 170.60 (2C=O), 157.59, 139.56, 130.48, 122.42. 115.46 (aromatic carbons), 57.53, 46.68 38.54, 22.57 (aliphatic carbons). HRMS-ESI (m/z) for  $\text{C}_{24}\text{H}_{25}\text{N}_3\text{O}_5\text{S}$ : 468.0785 (M-H), calculated, 467.5400.

### N-(3-((3-(4-Hydroxyphenyl)-1-oxo-1-(piperidin-1-yl)propan-2-yl)amino)-2-oxopropyl)benzenesulfonamide(12b)

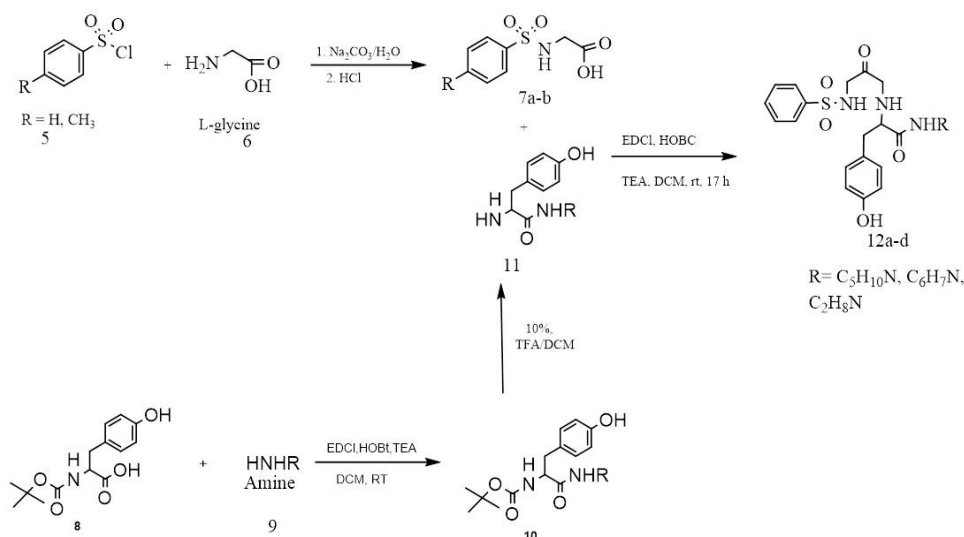
Yield 78%, Mp, 100°C. FTIR (KBr,  $\text{cm}^{-1}$ ): 3324 (NH), 3034 (C-H aromatics), 2929 (C-H aliphatic), 1684, 1625 (C=O of amide), 1438 (C=C aromatic), 1345, 1312 ( $-\text{SO}_2-$ ), 1241 (C-N).  $^1\text{H}$  NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 7.90 (d, 1H,  $\text{SO}_2\text{-NH}$ ), 7.70 - 7.60 (dd, 4H, Ar-H), 4.50 (s, 2H,  $\text{CH}_2$ ), 3.90 (s, 2H,  $[\text{CH}-\text{C}=\text{O}]$ ), 3.60 (s, 2H,  $\text{CH}_2$ -piperidine).  $^{13}\text{C}$ -NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 204.21 and 172.57 (2C=O), 153.61, 146.47, 132.35, 114.44 (aromatic carbons), 46.57, 36.54, 23.5, 23.57 (aliphatic carbons). HRMS-ESI (m/z) for  $\text{C}_{23}\text{H}_{29}\text{N}_3\text{O}_5\text{S}$ : 446.0385 (M-H) $^+$ , calculated, 445.5317.

### N-(3-((3-(4-Hydroxyphenyl)-1-oxo-1-(piperidin-1-yl)propan-2-yl)amino)-2-oxopropyl)-4-methylbenzenesulphonamide (12c)

Yield 85%, Mp, 100°C. FTIR (KBr,  $\text{cm}^{-1}$ ): 3324 (NH), 2929 (C-H aliphatic), 1684, 1625 (C=O of amide), 1430 (C=C aromatic), 1345, 1312 ( $-\text{SO}_2-$ ), 1244, 1088, (C-N).  $^1\text{H}$  NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 7.90 (d, 1H,  $\text{SO}_2\text{-NH}$ ), 7.60 (dd, 4H, Ar-H), 4.50 (s, 2H,  $\text{CH}_2$ ), 3.90 (s, 2H,  $[\text{CH}-\text{C}=\text{O}]$ ), 3.60 (s, 2H,  $\text{CH}_2$ -piperidine), 2.51 (s, 2H, Ar- $\text{CH}_3$ ).  $^{13}\text{C}$ -NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 204.81 and 172.54 (2C=O), 130.83, 115.42 (aromatic carbons), 63.57, 49.60, 38.52, 24.30.5, 21.5 (aliphatic carbons). HRMS-ESI (m/z) for  $\text{C}_{24}\text{H}_{31}\text{N}_3\text{O}_5\text{S}$ : 459.8267 ( $\text{M}^+$ ), calculated, 459.5681.

### 3-(4-Hydroxyphenyl)-N,N-dimethyl-2-((3-((4-methylphenyl)sulphonamido)-2-oxopropyl) amino)propenamide (12d)

Yield 92%, Mp, 120°C. FTIR (KBr,  $\text{cm}^{-1}$ ): 3324 (NH), 3060 (C-H aromatics), 2929 (C-H aliphatic), 1658 (C=O of amide), 1438 (C=C aromatic), 1390, 1308, ( $-\text{SO}_2-$ ), 1084, (C-N).  $^1\text{H}$  NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 9.20 (s, 1H, Ar-OH), 7.80 (d, 1H,  $\text{SO}_2\text{-NH}$ ), 7.60 (dd, 4H, Ar-H), 4.10 (s, 2H,  $\text{CH}_2$ ), 2.90 (s, 6H, N- $\text{CH}_3$ ), 2.50 (s, 3H, Ar- $\text{CH}_3$ ).  $^{13}\text{C}$ -NMR ( $\text{DMSO}_{d6}$ )  $\delta$ : 172.53 and 170.50 (2C=O), 137.47, 129.30, 115.43 (aromatic carbons), 54.52, 43.58, 38.64, 20.52 (aliphatic carbons). HRMS-ESI (m/z) for  $\text{C}_{21}\text{H}_{27}\text{N}_3\text{O}_4\text{S}$ : 419.7246 ( $\text{M}^+$ ), calculated, 419.4951.



**Figure 2:** Synthesis of Dipeptide bearing sulphonamide, reagents and conditions. (i) Na<sub>2</sub>CO<sub>3</sub>, H<sub>2</sub>O, -5°C - 0°C, r.t, 4 h. (ii) EDCI, HOBt, TEA, DCM, amine 17 h (iii) TFA/DCM (iv) EDCI, HOBt, TEA, 17 h.

### 3. Biological studies

#### 3.1. Anti-alzheimer's activity

The method of Yildiz *et al* (2022) [11] was applied to determine the anti-alzheimer's activity of the test sample as acetylcholinesterase and butylcholinesterase inhibitors. A volume of 100 mL of sodium phosphate buffer (0.1M, PH 7.0), 30 mL of the sample test and 40 mL of enzyme solution were mixed in microplate and incubated for 30 min at room temperature for 37°C. Subsequently 10 mL of 5,5 dithiobis-2 (2-nitrobenzoic acid) and 15 mL of acetylthiocholine or butyrylcholine iodide were added and absorbance was recorded. Galantamine was used as standard.

The percentage inhibition was determined using the following equation:

$$\text{Inhibition(\%)} = A_c - A_s \times A_c \times 100$$

Where,

$A_c$  = Absorbance of control

$A_s$  = Absorbance of sample.

The result was expressed as  $IC_{50}$

#### 3.2. Antioxidant activity by DPPH method

The new compounds were tested for their ability to scavenge free radicals using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) method established by Shen [12]. 3 mL of a 0.1 m Methanolic DPPH solution and 1.0 mL of this solution were mixed with 0.9 mL of methanol sample containing 0.8 mg of sulphonamide compounds at various concentrations and an individual reference medication (vitamin C). The reaction mixture was vigorously stirred before being left in the dark at room temperature for 30 minutes. Absorbance measurements at 517 nm were obtained after 30 min at room temperature.

$$\text{DPPH radical scavenging activity} = \frac{A_c - A_s}{A_c} \times 100 \text{ was used to calculate inhibition (\%).}$$

Where,

$A_c$  = Control absorbance,

$A_s$  = Sample absorbance

The concentration of compounds providing 50% inhibition ( $IC_{50}$ ) was calculated by plotting the graph of percentage inhibition against the concentration of compounds used.

## 4. Results And Discussion

#### 4.1. Chemistry

The synthesis of the sulfonamide dipeptides in Figure 2 was achieved by treating substituted benzenesulfonyl chloride (5) with L - glycine (6) in the presence of sodium carbonate to furnish (7a-7b). The treatment of boc-tyrosine (8) with different amines (9) gave compounds (10) which were deprotected to yield compound (11). The condensation reaction of compound (7a-7b) and compound (11) with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide HCl (EDC) in the presence of 1-hydroxybenzotriazole (HOBt) afforded the desired compounds (12a - 12d) in excellent yields. The synthesized compounds were characterized via FTIR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR and HRM spectroscopic analyses and the data obtained were in agreement with their assigned structures. In the infrared spectra of the dipeptides, the bands between 3324 and 3321  $cm^{-1}$  for N-H while 1684 and 1625  $cm^{-1}$  for carbonyl of the amide and 1354, 1338  $cm^{-1}$  for S=O respectively. In the <sup>1</sup>H-NMR spectra of the derivatives, the peaks at 7.12-7.1ppm were assigned to aromatic protons. The carbonyl peaks in the <sup>13</sup>C-NMR spectrum, appears between 170 and 172ppm and peaks ranging from 120-154.7 ppm for aromatic carbons. The high-resolution mass spectrometer (HRMS) peak of the derivatives appeared either as molecular ions ( $M^+$ ) or ( $M^-$ ). The results corresponded to the three decimals with the calculated values. The spectra used for the characterization of the new compounds are available as supporting material.

#### 4.2. Anti-alzheimer's Properties

**Table 1:** Results for anti-alzheimer's studies

Compounds	$IC_{50}$ mg/ml	
	AChE	BChE
12a	1.75	1.95
12b	0.60	0.65
12c	0.80	0.85
12d	1.52	2.20
Galantamine	0.70	0.70

The results of *in vitro* anti-alzheimer's studies reported in Table 1 as  $IC_{50}$  value revealed that the synthesized compounds showed good inhibition. Compound 12c have good inhibitory effect on the enzymes which showed a significant inhibition with  $IC_{50}$  value of 0.65 mg/mL when compared with  $IC_{50}$  value of galantamine (0.70 mg/mL). This implies that compound 12c is the most active candidate which may serve as useful lead compounds in search for powerful anti-alzheimer's agents.

### 4.3. Antioxidant properties

**Table 2:** Antioxidant (% scavenging and IC<sub>50</sub> values) of the synthesis compounds

Compds	% inhibition 50 mg / mL	% inhibition 25 mg/mL	% inhibition 12.5 mg/mL	IC <sub>50</sub> (mg/mL)
12a	93.62 ± 0.33	92.82 ± 0.12	94.76 ± 0.42	1.29
12b	93.86 ± 0.31	85.87 ± 0.42	78.80 ± 0.47	0.76
12c	87.11 ± 0.52	93.24 ± 0.32	91.31 ± 0.21	1.62
12d	72.13 ± 0.45	74.90 ± 0.52	84.25 ± 0.40	1.59
Vitamin C	95.88 ± 0.44	90.78 ± 0.40	89.44 ± 0.41	0.79

All the synthesized compounds in Table 2 exhibited antioxidant properties that can prevent the progress of oxidative stresses. Compound 12a and 12b had better antioxidant properties. Compound 12a and 12b (93.86 and 93.62.76% inhibition at 50 mg/mL) had comparable to antioxidant property as vitamin C (95.88% inhibition at 50 mg/mL). It is note that the lower the IC<sub>50</sub> value implies better antioxidant potential. The IC<sub>50</sub> value of compound 12b (0.76 mg/mL) is comparatively almost the same with that of vitamin C (0.79 mg/mL). This shows that compound 12b can be serve as antioxidant agent.

## 5. Conclusion

In conclusion, seven novel Gly-Tyro dipeptide sulphonamoyl carboxamides bearing moieties of pharmacological importance were synthesized and successfully characterized using spectroscopic techniques. The assigned structures complied with the spectral data. Compound 12c were found to be the most potent agent which may serve as useful lead compounds in search for powerful anti-alzheimer's agents while Compounds 12c have the most active antioxidant activity and might be considered the most promising agent.

### Article Information

**Acknowledgments:** Our unreserved gratitude goes Prof. U.C. and all those who contributed to the success of this research and presentation of this manuscript.

**Author Contributions:** I.O.C. - Conceptualization, Methodology, Formal analysis, Writing – original draft; O.U.C. - Methodology, Writing – review & editing, Supervision; O.C.C. - Data curation, Formal analysis.

**Funding / Financial Support:** The authors received no external funding.

**Conflict of Interest (Competing Interests):** The authors have declare that no competing interests exists.

**Ethical Approval:** Not Applicable.

**Informed Consent:** Not Applicable.

**Data Availability Statement:** Not Applicable.

**Disclaimer (Artificial Intelligence):** The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

## References

- [1] E. A. Onoabedje, A. Ibezim, U. C. Okoro, and S. Batra. Synthesis, molecular docking, antiparasitic and antioxidant activities of new sulfonamido-peptide derivatives. *Heliyon*, 6(9):e04958, 2020.
- [2] L. R. Meena, V. S. Sharma, and P. Swarnkar. Synthesis, biological investigations, QSAR and DFT analysis of sulfonamide chalcones as potential: antimicrobial, antifungal and antimalarial agents. *World Sci. News*, 147:179–196, 2020.
- [3] B. S. Aronimo, U. C. Okoro, R. Ali, C. U. Ibeji, J. A. Ezugwu, and D. I. Ugwu. Synthesis, molecular docking and antimalarial activity of phenylalanine-glycine dipeptide bearing sulphonamide moiety. *J. Mol. Struct.*, 1246:131201, 2021.
- [4] D. Ugwuja, U. Okoro, S. Soman, R. Soni, S. Okafor, and D. Ugwu. New peptide derived antimalaria and antimicrobial agents bearing sulphonamide moiety. *J. Enzyme Inhib. Med. Chem.*, 34(1):1388–1399, 2019.
- [5] D. Ugwu, U. Okoro, P. Ukoha, S. Okafor, A. Ibezim, and N. Kumar. Synthesis, characterization, molecular docking and in vitro antimalarial properties of new carboxamides bearing sulphonamide. *Eur. J. Med. Chem.*, 135:349–369, 2017.
- [6] H. A. Grab, V. C. Kirsch, S. A. Sieber, and T. Bach. Total synthesis of the cyclic decapeptide vioprolide D via its (Z)-diastereoisomer. *Angew. Chem. Int. Ed.*, 59(30):12357–12361, 2020.
- [7] H. Okita, Y. Kato, T. Masuzawa, K. Arai, S. Takeo, K. Sato, N. Mase, T. Oyoshi, and T. Narumi. Stereoselective synthesis of Gly-Gly-type (E)-methylalkene and (Z)-chloroalkene dipeptide isosteres and their application to 14-mer RGG peptide mimetics. *RSC Adv.*, 10(49):29373–29377, 2020.

- [8] J. A. Ezugwu, U. C. Okoro, M. A. Ezeokonkwo, C. R. Bhimapaka, S. N. Okafor, D. I. Ugwu, O. C. Ekoh, and S. I. Attah. Novel Leu-Val based dipeptide as antimicro-bial and antimalarial agents: synthesis and molecular docking. *Front. Chem.*, 8:583926, 2020.
- [9] S. I. Attah, U. C. Okoro, S. P. Singh, C. C. Eze, C. U. Ibeji, J. A. Ezugwu, O. U. Okenyeka, O. Ekoh, D. I. Ugwu, and F. U. Eze. Pro-Gly based dipeptide containing sulphonamide functionality, their antidiabetic, antioxidant, and anti-inflammatory activities. Synthesis, characterization and computational studies. *J. Mol. Struct.*, 1264:133280, 2022.
- [10] A. Pradeepkiran, P. A. Reddy, and P. H. Reddy. *Pharmacophore based models fortherapeutic drugs against phosphoryl tau in Alzheimer's disease, Drug Discovery Today vol 24.* vol 24, 2019.
- [11] M. Yıldız, M. Bingul, Y. Zorlu, M. F. Saglam, M. Boga, M. Temel, M. S. Koca, H. Kandemir, and I. F. Sengul. Dimethoxyindoles Based Thiosemicarbazones as Multi-Target Agents: Synthesis, Crystal Interactions, Biological Activity and Molecular Modeling. *Bioorganic Chemistry*, 120:105647, 2022. doi: 10.1016/j.bioorg.2022.105647.
- [12] Z. G. Jiao, H. Q. He, C. C. Zeng, J. J. Tan, L. M. Hu, and C. X. Wang. Design, synthesis and anti-HIV integrase evaluation of N-(5-chloro-8-hydroxy-2-styrylquinolin-7-yl)benzenesulphonamide derivatives. *Molecules*, 15:1903–1917, 2010.