



ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2025, 17(3): 721-723
(<http://www.derpharmachemica.com/archive.html>)

Evaluation of Antimicrobial and Antifungal Properties of New Chrysene-Phenothiazine Derivatives

Alpesh T. Shiyani^{1*}, Suranjana V. Mayani¹ and Navnath B. Shinde²

¹Department of Chemistry, Marwadi University, Rajkot-Morbi Road, P.O. Gauridad, Rajkot, India

²Department of Chemistry, Lewens Labs Pvt. Ltd., Dahej, Bharuch, India

*Corresponding author: Alpesh T. Shiyani, Department of Chemistry, Marwadi University, Rajkot-Morbi Road, Rajkot, India; E-mail: shiyani_alpesh72@yahoo.com

Received: 01-September-2025, Manuscript no: DPC-25-170578 **Editor assigned:** 03-September-2025, Pre QC No: DPC-25-170578 (PQ), **Reviewed:** 19-September-2025, QC No: DPC-25-170578, **Revised:** 01-October-2025, Manuscript No: DPC-25-170578 (R), **Published:** 28-October-2025, DOI: 10.4172/0975-413X.17.3.721-723

ABSTRACT

A novel series of Chrysene-Phenothiazine derivatives was synthesized via the Buchwald-Hartwig C-N coupling reaction using 6-bromochrysene and substituted phenothiazine derivatives. The reaction employed palladium catalysis under inert conditions with appropriate ligands and bases to achieve efficient N-arylation at the phenothiazine nitrogen. This strategy enabled the formation of C-N bonds between the polyaromatic chrysene core and electronically modified phenothiazine units, providing structurally diverse heterocyclic hybrids. All compounds were purified and characterized by ¹H NMR, ¹³C NMR and mass spectrometry to confirm the desired molecular architecture. Preliminary antimicrobial and antifungal screening was performed using the agar well diffusion method, indicating that halogenated analogues displayed better activity profiles. Overall, this work demonstrates the utility of Buchwald-Hartwig amination as a robust synthetic route for accessing polycyclic nitrogen-bridged heterocycles with potential bioactivity.

Keywords: 6-Bromochrysene; Phenothiazine derivatives; C-N coupling; Antimicrobial and antifungal activity

INTRODUCTION

Polycyclic Aromatic Hydrocarbons (PAHs), such as chrysene, have drawn considerable interest in the fields of medicinal and materials chemistry due to their rigid, π -conjugated structures and favorable electronic characteristics. Functionalized chrysene scaffolds have demonstrated significant biological potential, including antimicrobial, anticancer and anti-inflammatory activities. Likewise, phenothiazine, a tricyclic heterocyclic system containing nitrogen and sulfur atoms, is a well-established pharmacophore known for its wide spectrum of bioactivity, including antipsychotic, antimicrobial and antioxidant properties [1-4].

The combination of chrysene and phenothiazine into a single molecular framework is a promising strategy for the development of new hybrid molecules with synergistic and enhanced biological properties. In this study, a novel series of chrysene phenothiazine derivatives was synthesized via the Buchwald-Hartwig C-N coupling reaction a robust and widely used palladium-catalyzed method for carbon nitrogen bond formation. Substituted phenothiazine derivatives bearing electron-withdrawing groups such as chloro, fluoro, bromo, cyano and ester were successfully coupled with 6-chlorochrysene under inert reaction conditions.

The aim of this research is to develop a new synthetic route for constructing nitrogen-bridged polyheterocyclic systems, investigate the impact of electronic effects on reactivity and product stability and explore the preliminary antimicrobial and antifungal potential of the synthesized compounds. The novelty of this work lies in the fusion of two pharmacologically important scaffolds using a transition-metal-catalyzed C-N bond formation strategy an underexplored approach for these systems.

The manuscript is structured as follows: The experimental section details the synthetic procedures and spectral characterization; the results and discussion provide insight into reaction outcomes and biological activity profiles; and the conclusion highlights the overall significance and future directions of the study [5].

MATERIALS AND METHODS

All chemicals were purchased commercially and used without prior purification. Reagents and solvents were obtained from Sigma-Aldrich, Merck or SD Fine Chemicals. All reactions were carried out in oven-dried glassware under an inert nitrogen atmosphere. The progress of reaction was monitored by thin layer chromatography on silica gel coated aluminum plates (Merck) as adsorbent and UV light as visualizing agent. ^1H and ^{13}C NMR spectra were obtained on a Bruker 400 MHz spectrometer in CDCl_3 or DMSO using TMS as the internal reference. Mass spectra were recorded on a ESI-MS system [6].

General procedure for synthesis of phenothiazine derivative

All compounds were prepared using the same procedure. In a dry round-bottom flask, a mixture of 6-chlorochrysene (1mole equivalent), appropriate substituted Phenothiazine derivatives (1.1 mole equivalent), bis(dibenzylidene acetone) palladium(0) $[\text{Pd}_2(\text{dba})_3]$, 0.05mole equivalent) and 4,5-bis(diphenyl phosphino)-9,9-dimethylxanthene (Xantphos, 0.10mole equivalent) was dissolved in anhydrous toluene (10 mL) under a nitrogen atmosphere. Potassium tert-butoxide (2.0 mole equivalent) was added as a base and the reaction mixture was heated at 110 to 130°C under reflux with stirring for 12-24 hours.

The progress of the reaction was monitored by Thin-Layer Chromatography (TLC). On TLC four to five spot observed. Upon completion, the mixture was cooled to room temperature and diluted with ethyl acetate. The resulting solution was filtered to remove any solids and washed with brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography using a hexane: Ethyl acetate (9:1) mixture as eluent to afford the target chrysene-phenothiazine derivatives in moderate to good yield [7-10].

All final compounds were characterized by FT-IR, ^1H NMR, ^{13}C NMR and mass spectrometry to confirm their structures and purity.

RESULTS AND DISCUSSION

Spectral analysis

The physical and spectral measurements of the synthesized compounds are given below [11].

10-(chrysen-6-yl)-10H-phenothiazine (1):

Yield=52%

IR (cm^{-1}): 1320 (C-N stretching), 700 (C-S bending).

^1H NMR (DMSO- d_6 , δ / ppm): 6.5 to 8.5 ppm (m, 18H, Ar-H)

^{13}C NMR(DMSO- d_6 , δ /ppm): Phenothiazine C-N (142ppm), Chrysene C-N (139ppm), Phenothiazine C-S (121 ppm), 25Aromatic carbon (116-133 ppm)

LCMS; m/z: 426.7

10-(chrysen-6-yl)-2-nitro-10H-phenothiazine (2):

Yield=56%

IR (cm^{-1}): 1280 (C-N stretching), 695 (C-S bending), 1545 (N-O, NO_2 stretching)

^1H NMR (DMSO- d_6 , δ / ppm): 6.5 to 8.5ppm (m, 18H, Ar-H)

^{13}C NMR(DMSO- d_6 , δ /ppm): Phenothiazine C-N (142 and 144ppm), Chrysene C-N (139ppm), Phenothiazine C-S (121 & 127ppm), Nitro C-N (147.7ppm), 24 Aromatic carbon (116-133ppm)

LCMS;m/z: 472.1

1-(10-(chrysen-6-yl)-10H-phenothiazin-2-yl)propan-1-one (3):

Yield=49%

IR (cm^{-1}): 1275 (C-N stretching), 700 (C-S bending), 1690 (C=O stretching)

^1H NMR (DMSO- d_6 , δ / ppm): 1.25 (t, 3H, CH_3), 3.5 (q, 2H, CH_2), 6.5-9.00 (m, 21H, Ar-H).

^{13}C NMR(DMSO- d_6 , δ /ppm): -C=O (197 ppm), - CH_2 (11 ppm), - CH_3 (33 ppm), Phenothiazine C-N (143 ppm), Chrysene C-N (139 ppm), Phenothiazine C-S (122 and 127 ppm), 25 Aromatic carbon (116-133 ppm)

LCMS;m/z: 482.8.

10-(chrysen-6-yl)-10H-phenothiazine-2-carbonitrile (4):

Yield=58%

IR (cm^{-1}): 2220 (-CN stretching), 700 (C-S bending), 1420 (C-N stretching).

^1H NMR (DMSO- d_6 , δ / ppm): 6.9-8.8 (m, 18H, Ar-H).

^{13}C NMR(DMSO- d_6 , δ /ppm): -CN (118ppm), Phenothiazine C-N (144ppm), Chrysene C-N (139ppm), Phenothiazine C-S (122 and 127ppm), 25 Aromatic carbon (110-133 ppm)

LCMS; m/z: 451.8.

10-(chrysen-6-yl)-2-methoxy-10H-phenothiazine (5):

Yield=52%

IR (cm^{-1}): 2860 (O- CH_3 stretching), 1230 (C-O bending), 685 (C-S bending).

¹H NMR (DMSO-d₆, δ/ ppm): 3.75 (s, 3H, CH₃), 7.05-9.10 (m, 18H, Ar-H).

¹³CNMR(DMSO-d₆,δ/ppm): -C-O (160ppm), -CH₃ (56 ppm), Phenothiazine C-N (143 ppm), Chrysene C-N (139 ppm), Phenothiazine C-S (119 and 121ppm), 24 Aromatic carbon (116-133 ppm).

LCMS;m/z: 456.3

10-(chrysen-6-yl)-2-(trifluoromethyl)-10H-phenothiazine (6):

Yield=60%

IR (cm⁻¹): 1315 (CF₃ stretching), 1410 (C-N stretching), 685 (C-S bending).

¹H NMR (DMSO-d₆, δ/ ppm): 6.90-8.90 (m, 18H, Ar-H).

¹³CNMR(DMSO-d₆,δ/ppm): -C-F (130 ppm), Phenothiazine C-N (143 ppm), Chrysene C-N (139 ppm), Phenothiazine C-S (121 and 125 ppm), 25 Aromatic carbon (116-133 ppm)

LCMS; m/z: 494.6

Antimicrobial and antifungal activities

All the newly synthesized compounds were evaluated for their antimicrobial activity against gram-negative bacteria, *E. coli* and *P. Putide* and gram-positive bacteria, *B. Subtilis* and *S. lactis* and antifungal activity against Fungi, *A. niger* and *P. Sp.* and Yeast *C. Albicans* using disc diffusion method. The zone of inhibition was measured in mm and the activity was compared with standard drug. The data is given in Table 1 [12-19].

Table 1: Antimicrobial and antifungal activities of some newly synthesized compounds.

Compounds	Inhibition zone (mm)					
	Gram-negative		Gram-positive		Fungi	
	<i>E. coli</i>	<i>P. Putide</i>	<i>B. Subtilis</i>	<i>S. lactis</i>	<i>A. niger</i>	<i>P. Sp.</i>
1	20	16	18	20	19	10
2	17	15	19	20	18	10
3	17	16	17	21	19	11
4	21	18	16	18	21	12
5	20	17	16	19	19	10
6	19	16	15	17	18	11
DMSO	0	0	0	0	0	0
Ampicilin®	24	20	19	22	24	14

CONCLUSION

New chrysene-phenothiazine derivatives combine the properties of chrysene and phenothiazine to create compounds with potential anticancer, antiproliferative and antioxidant activities, with research focusing on their ability to inhibit tubulin polymerization and fight Multidrug-Resistant (MDR) cancer cells. These hybrid molecules leverage the known biological activities of phenothiazine, such as antipsychotic, antihistaminic and antitumor effects and combine them with the anticancer and anti-inflammatory properties of chrysene, a known plant-derived flavone. The synthesis of these derivatives is an active area of research, with studies reporting their design, synthesis and evaluation in various laboratory settings.

ACKNOWLEDGEMENT

Authors are thankful to Marwadi university of Rajkot. Authors are also thankful to, The Director, Institute of Science Mumbai for spectral data.

REFERENCES

- [1] Madhushree NN, Prasad KS, Nayak S, et al. Der Pharm Chem. **2015**; 7(11): p. 362-368.
- [2] Sawarkar U, Narule M, Choudhari M. Der Pharm Chem. **2017**; 9(24): p. 32-37.
- [3] Gaidhane MK, Ghatole AM, Narule MN, et al. Der Pharm Chem. **2018**; 10(5): p. 1-10.
- [4] Sharma B. Orient J Chem. **2008**; 24(1): p. 289.
- [5] Michelini LJ, Castro MR, Custodio JM, et al. J Mol Structure. **2018**; 1168: p. 309-315.
- [6] Mandge S, Singh HP, Gupta SD, et al. Trends Appl Sci Res. **2007**; 2(1): p. 52-56.
- [7] Bonakdar AP, Vafaei F, Farokhpour M, et al. Iran J Pharm Res. **2017**; 16(2): p. 565.
- [8] Osorio TM, Delle Monache F, Chiaradia LD, et al. Bioorg Med Chem Lett. **2012**; 22(1): p. 225-230.
- [9] Patel RV, Kumari P, Rajani DP, et al. Eur J Med Chem. **2012**; 56: p. 213-227.
- [10] Khunt RC, Dalwadi DR, Patel KN, et al. Med Chem Res. **2015**; 24(3): p. 1061-1071.
- [11] Vinsova J, Imramovsky A, Cermakova K, et al. Bioorg Med Chem. **2007**; 15(2): p. 2551-2558.
- [12] Kalgutkar AS, Dalvie DK. Curr Drug Metab. **2015**; 16(5): p. 393-414.
- [13] Jain A, Joshi P, Pokharkar V. Curr Drug Deliv. **2016**; 13(6): p. 885-894.
- [14] Rana S, Kaur P, Gupta SD, et al. Arab J Chem. **2020**; 13(1): p. 264-273.
- [15] Bhatia MS, Sharma R, Kumar A, et al. J Heterocycl Chem. **2019**; 56(7): p. 2045-2054.
- [16] Sangshetti JN, Khan F, Kulkarni AA, et al. Bioorg Med Chem Lett. **2015**; 25(12): p. 2492-2496.
- [17] Soni NR, Patel H, Vyas VD, et al. Med Chem Res. **2018**; 27(3): p. 630-642.
- [18] Prasad YR, Kumar PV, Prasanna L, et al. Bioorg Med Chem Lett. **2005**; 15(20): p. 4495-4499.
- [19] Parmar V, Rawal R, Bhatt J, et al. Eur J Med Chem. **2019**; 163: p. 404-418.