Synthesis of Thiophene-1,3,4-Thiadiazole and Thiophene-1,3-Thiazole Hybrids as Candidates for Antileishmanial Agents

Deysiane Lima Salvador (PG), Celso Vataru Nakamura (PQ), Fernanda Andreia Rosa (PQ), Maria Helena Sarragiotto (PQ)
Department of Chemistry - State University of Maringá, 87020-900, Maringá – PR, Brazil
deyssiane_salvador@outlook.com

Studies reported in literature have demonstrated that compounds containing the thiophene nucleus with different substituents at positions -2 and -5, or coupled to other heterocyclic (Figure 1) present antileishmanial activity. Also, derivatives containing the 1,3,4-thiadiazole and 1,3-thiazole nucleus have shown impressive antimicrobial and antiparasitic activities.

Figure 1. Thiophene derivatives with leishmanicidal activity.

In our previous work, a series of pyrazolo[3,4-d]pyridazinone-N-acylhydrazone-(bi)thiophene hybrids with antileishmanial activity were synthesized by using molecular hybridization strategy. In continuing our studies, in the present work we describe the synthesis thiophene-1,3,4-thiadiazole and thiophene-1,3-thiazole hybrids as candidates for antileishmanial agents.

To obtain the thiophene derivatives containing the nucleus 1,3,4-thiadiazole (5a-b) and 1,3-thiazole (6a-b), the corresponding aldehyde was submitted to reaction with thiosemicarbazide, giving the intermediates 4a-b.

Scheme 1. Synthetic route for preparation of 5a-b and 6a-b.

The derivatives 5a-b were prepared by reacting 4a-b with FeCl₃,6H₂O (cat.) in ethanol. The 1,3-thiazoles 6a-b were obtained by reaction of 4a-b with bromoacetophenone in isopropanol. Compounds 5b and 6b are not reported in the literature.

The products 5a-b and 6a-b were obtained with yields in the range of 70-90%, and were characterized by spectroscopic analysis of ¹H and ¹³C NMR.

In summary, we synthesized a series of thiophene derivatives coupled to different heterocyclic nucleus, as potential antileishmanial agents.

ACKNOWLEDGEMENTS
DQI-UEM, CAPES, CNPq, Fundação Araucária.

REFERENCES