Apr 5th, 8:00 AM - 12:00 PM

Synthesis of 2-Carbamoyl-4-Oxo-1,5-Diazabicyclo[3.2.1] Octane Derivatives as a Possible Inhibitors of Serine β-Lactamases

Haiyu Wang

Abbas Shilabin
East Tennessee State University

Follow this and additional works at: https://dc.etsu.edu/asrf
Synthesis of 2-Carbamoyl-4-oxo-1,5-diazabicyclo[3.2.1] octane Derivatives as Possible Inhibitors of Serine β-Lactamases

Haiyu Wang and Dr. Abbas G. Shilabin
Department of Chemistry, East Tennessee State University, Johnson City, TN 37614, U.S.A.

ABSTRACT
Antibiotic resistance is becoming ever more severe due in part to the increasing use of antibiotic drugs. One significant contributor to this problem is the production of β-lactamase enzymes that provide resistance to common β-lactam antibiotics such as penicillin. The scope of this research is to synthesize and study the β-lactamase inhibitors of 2-carbamoyl-4-oxo-1,5-diazabicyclo[3.2.1] octane derivatives. β-lactamase inhibitors can inhibit the functional inhibition of bacterial β-lactam and aid in the prevention of hydrolysis. Currently the research process in the beginning stages of synthesizing three compounds: (R)-hexahydro-6-oxopyrimidine-4-carboxylic acid (3a), hexahydro-2,2-dimethyl-6-oxopyrimidine-4-carboxylic acid (3b) and hexahydro-6-oxo-2-phenylpyrimidine-4-carboxylic acid (3c).

RESULTS

EXPERIMENTAL PROCEDURE

Compound 1a: To a solution of D-asparagine (3.1526 g) in 400 mL water at 45 °C, add 16.25 mL of 37% formaldehyde. After stirring for 10 hours at 45°C the solution was cooled down to 5°C to give a white slurry. The slurry was allowed to warm up to 25°C, then the precipitate collected by vacuum filtration. The compound then put into oven to dry for over night.

Class C lactamases (e.g. AmpC) which are encoded by bla genes on the chromosome are important enzymes in clinical diagnostics. AmpC lactamases are sensitive to oxacillin, amoxicillin and cloxacillin, but are typically resistant to cephamycins, cephalosporins and penicillin. Ty150 can activate Ser67 by attacking lactam ring in a hydrolysis process as general base.

Compound 2b: To a mixture of D-asparagine (2 g, 8 mmol) in HPLC grade acetonitrile (12 mL), KOH (4.01 g, 0.55 g, 8 mmol) was added into the reaction. The reaction was done with oil bath at 120 °C, then do reflux for 10 hours, magnetic stirring rate set at 400 rpm.

EXPERIMENTAL PROCEDURE

CONCLUSION

The authors acknowledge the Department of Chemistry and The School of Graduate Studies at ETSU. We are also grateful for the financial support of the ETSU Office of Research and Sponsored Programs Administration (ORSPA).

ACKNOWLEDGEMENTS

REFERENCES