

New Mono, Bis-2,2-(arylidineaminophenyl)benzimidazoles: Synthesis and Antimicrobial Investigation

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Antibacterial activity

Antibacterial testing was performed by cup plate method.³⁷ Nutrient broth was prepared by dissolving peptone (0.5%), yeast extract (0.15%), beef extract (0.15%), sodium chloride (0.36%), and monopotassium phosphate (0.13%) in distilled water (100 mL). The pH of the solution was adjusted to 7.2 by adding sodium hydroxide solution (4%) and the resulting solution was autoclaved for 20 minutes at 15 psi. One day prior to the experiment, the cultures against *Staphylococcus aureus*, *Bacillus subtilis*, *Streptococcus pyogenes*, *Salmonella typhimurium*, *Escherichia coli* and *Klebsiella pneumonia* were inoculated in nutrient broth (inoculation medium) and incubated overnight at 37 °C. Nutrient agar medium was prepared by dissolving peptone (1%), yeast extract (0.6%), beef extract (0.5%), and sodium chloride (0.5%) in distilled water. The pH of the solution was adjusted to 7.2 by adding 4% aqueous sodium hydroxide solution. Agar (2.4%) was then added and the whole solution was autoclaved for 20 minutes at 15 psi. Preliminary screening for ten quinazolines was performed at fixed concentrations of 1000

µg/ml. Inoculation medium containing 24-hours grown culture was added aseptically to the nutrient medium and mixed thoroughly to get the uniform distribution. This solution was poured (25 mL in each dish) into Petri dishes and then allowed to attain room temperature. Thereafter, six millimeter wide bores were made on the agar using a borer. The solutions of test samples were added into each of the bores using a sterile tip with micropipette. Ampicillin was used as the standard and DMSO as the solvent control. The test samples and the standard were tested at a concentration of 1000 µg. The plates were allowed to stand for an hour in order to facilitate the diffusion of the drug solution. Then the plates were incubated at 37 °C for 48 hours. The zones of inhibition against all the microorganisms were measured in millimeters.

Antifungal activity

The antifungal activity of quinazoline compounds were tested against the pathogenic fungi *Aspergillus niger*, *Candida albicans* and *Trichoderma viridae* by cup-plate

Table 1. MIC values of potent mono, bis-2-o-(arylidineaminophenyl)benzimidazoles and standard drugs towards bacteria.

| Compound | MIC (µg/mL) | | | | | |
|-----------|------------------------|--------------------|--------------------|------------------------|----------------|---------------------|
| | Gram-positive bacteria | | | Gram-negative bacteria | | |
| | <i>S. aureus</i> | <i>B. subtilis</i> | <i>S. pyogenes</i> | <i>S. typhimurium</i> | <i>E. coli</i> | <i>K. pneumonia</i> |
| 5 | 5 | 15 | 15 | 20 | 25 | 15 |
| 6 | 10 | 10 | 10 | 15 | 20 | 20 |
| 13 | 5 | 10 | 10 | 10 | 5 | 10 |
| 14 | 5 | 2.5 | 5 | 2.5 | 10 | 10 |
| 15 | 2.5 | 5 | 2.5 | 2.5 | 5 | 2.5 |
| 16 | 2.5 | 2.5 | 5 | 2.5 | 2.5 | 5 |
| A | 10 | 20 | 25 | 10 | 15 | 10 |

Table 2. MIC values of potent bis-2-o-(arylidineaminophenyl)benzimidazoles and standard drugs towards fungi.

| Compound | MIC (µg/mL) | | |
|---------------------|-----------------|--------------------|-------------------|
| | <i>A. niger</i> | <i>C. albicans</i> | <i>T. viridae</i> |
| 13 | 10 | 20 | 15 |
| 14 | 10 | 15 | 10 |
| 15 | 5 | 5 | 5 |
| 16 | 5 | 2.5 | 2.5 |
| Ketoconazole | 15 | 25 | 20 |

method.³⁷ Nutrient agar medium was prepared by the same method as explained under evaluation of antibacterial activity. One and half day prior to the experiment, the fungal cultures of *A. niger*, *C. albicans* and *T. viridae* prepared in the inoculation medium were incubated at 37 °C for 36 hours. The fungal medium was prepared by dissolving peptone (0.5%), sodium chloride (0.36%), monopotassium phosphate (0.13%), and glucose (2%) in distilled water (100 mL). The pH of the solution was adjusted to 7.2 by adding sodium hydroxide solution (4%)

and the resulting solution was autoclaved for 20 minutes at 15 psi. This was cooled to 45–50 °C with gentle shaking. One and half day, grown cultures were added aseptically to this medium and mixed thoroughly to get uniform distribution. The solutions of the test samples and standard were evaluated for antifungal activity by cup-plate method at a concentration of 1000 µg. The zone of inhibition was measured in millimeter for the particular test sample with each organism at 48 hours interval. Ketoconazole was used as the standard.

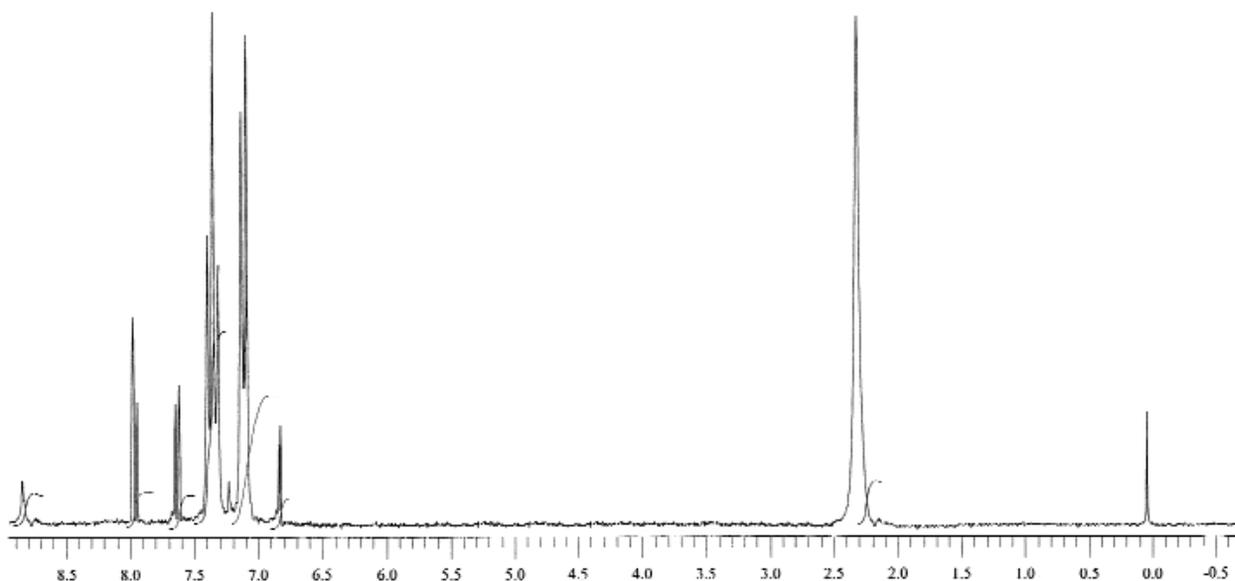


Fig. 1. ¹H-NMR spectrum of compound (1)

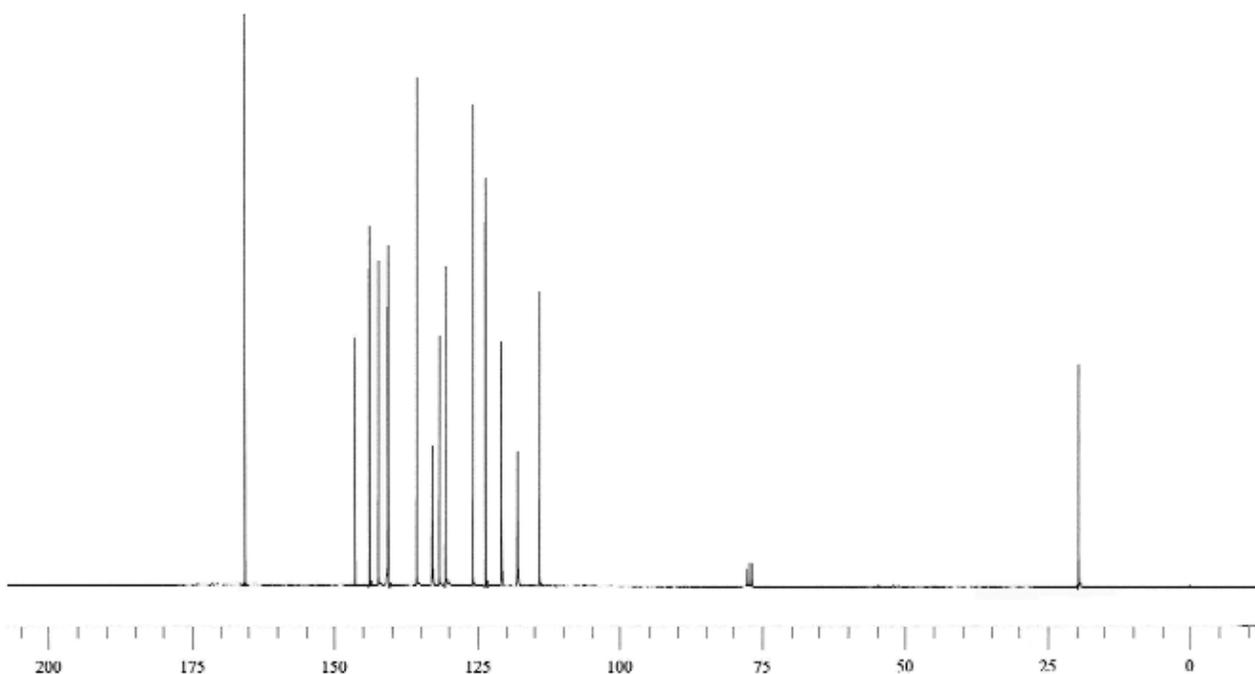


Fig. 2. ¹³C-NMR spectrum of compound (1)

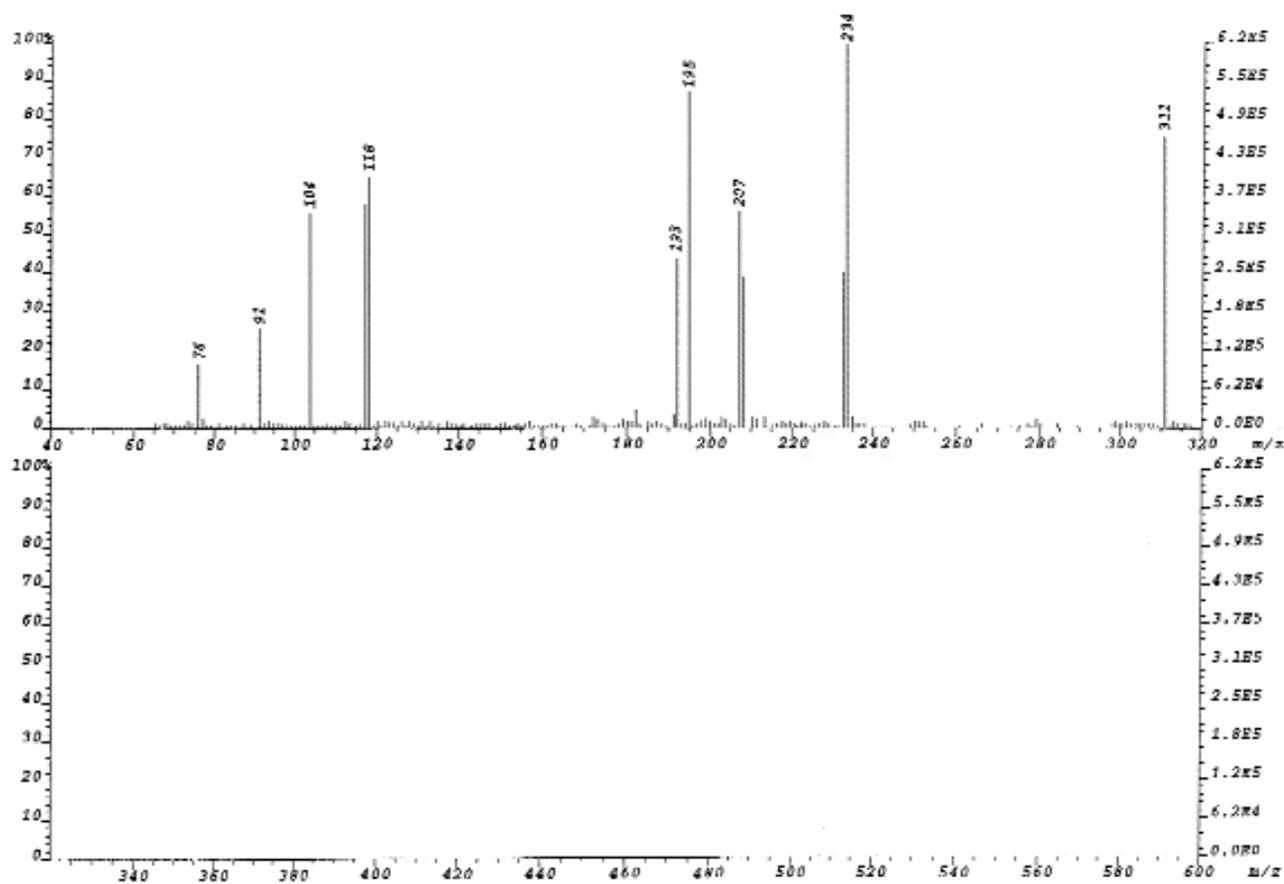
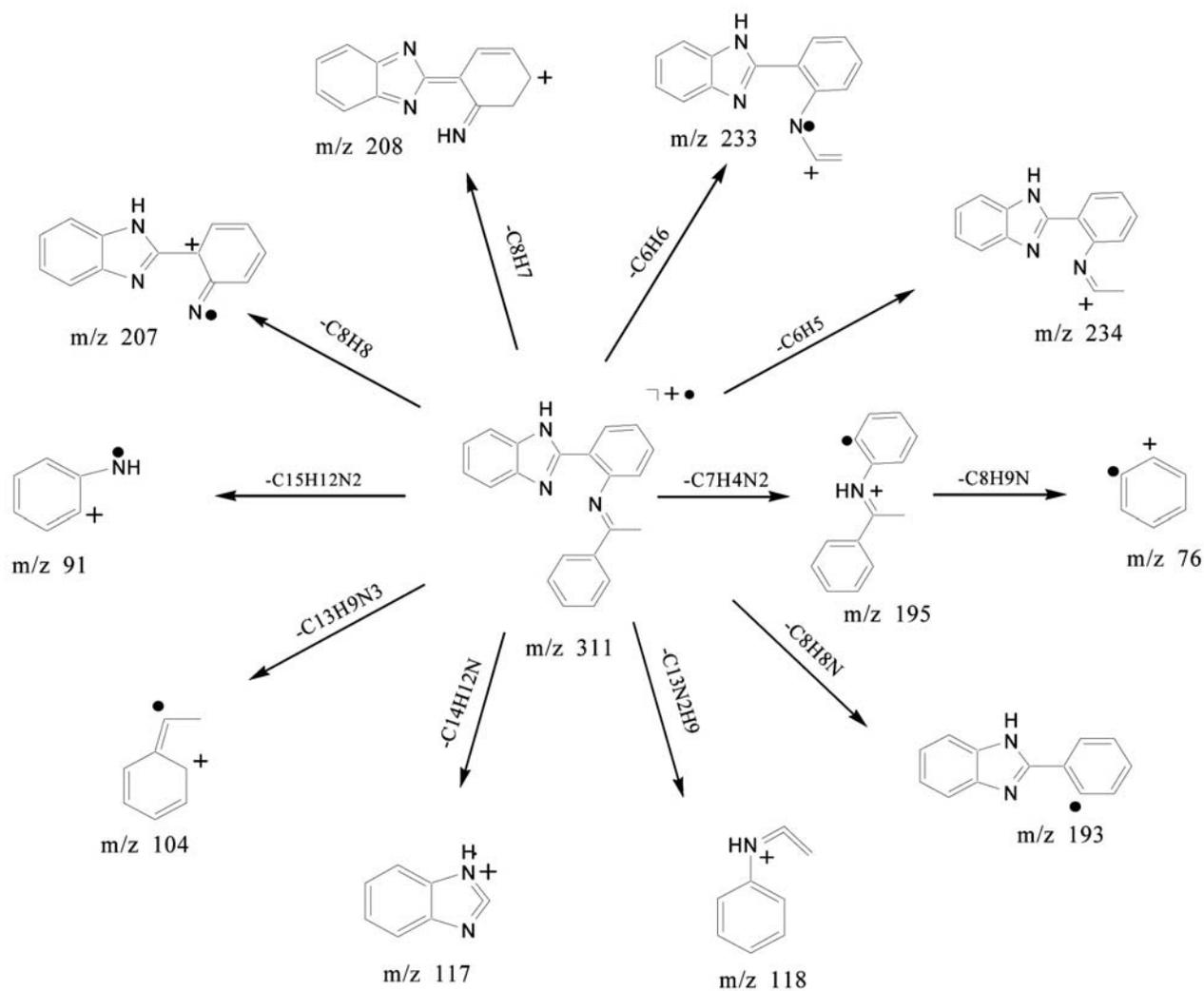


Fig. 3. FAB mass spectrum of compound (1)



Scheme 1. FAB mass fragmentation pattern of N-[2-(1H-benzo[d]imidazol-2-yl)phenyl]-N-[(E)-1-phenylethylidene]amine (**1**).