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## Application response surface methodology for determination optimization of trace zinc in environmental samples by adsorptive stripping voltammetry

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Adsorptive stripping voltammetry is one of the stripping voltammetry method that is widely used in the analysis of heavy metals because it has good sensitivity. metals with very small concentrations can be analyzed. The purpose of this study was to obtain the optimum condition of the Zn metal ions simultaneously. To achieve these objectives. required an optimization technique of analytical procedures by using Response Surface Methodology with Central Composite Design (CCD). The research design was used in this study is a CCD with 4 variables. 3 level and 31 a combination of treatments. The first step of 2k factorial design optimization are: to give the highest level of code values (+1). the lowest level (-1) and code (0) as the center point. Programs that will be used for statistical data processing. namely Mini Tab using RSM. Based on data analysis with response surface method. the obtained optimum conditions for the determination of zinc is: calcon concentration of 0.71 mmol/L; pH = 7.18; accumulation potential -0.56 V and the accumulation time 62.16 s. From the results obtained optimum conditions RSD of 2.5% with a recovery of 98.01%. respectively. Limit of Detection (LOD) for Zn(II) was 1.21 ( $\mu\text{g/L}$ ). RSM has been successfully applied to the determination of Zn in environmental samples fast and effectively.

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## Synthesis of methane-linked bis-heterocycles containing the 1,5-disubstituted-tetrazole moiety via Ugi-azide based methodologies

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Bis-heterocycles are structurally complex compounds having two linked, fused, merged or bound heterocyclic frameworks,<sup>1</sup> which have attracted much attention of synthetic community due to their potential applications in agrochemistry, optics, material science, and medicinal chemistry.<sup>2</sup> Moreover, 1,5-disubstituted-tetrazoles (1,5-DS-T's) are known as resistant bioisosters of the *cis*-amide bond of peptides,<sup>3</sup> which are present in numerous valuable drugs like the 3<sup>rd</sup> generation cephalosporin antibiotic Latamoxeb.<sup>4</sup> Besides, 1,5-DS-T's are suitable precursors of a plethora of MOF's and chelating agents.<sup>5</sup> Thus, according to our ongoing program to develop short and versatile Ugi-azide based methodologies toward a variety of methane-linked bis-heterocycles containing the 1,5-DS-T moiety, we herein show our most recent published results. In 2013, we described the synthesis of azepino[4,5-*b*]indol-4-one-1,5-1H-tetrazoles in two steps: i) one pot (Ugi-azide/N-acylation/SN<sub>2</sub>), and ii) free radical mediated cyclization, as well as *in silico* studies as 5-Ht6R ligands using docking techniques (Figure 1a).<sup>6</sup> In 2014, we reported the synthesis of 2,3,4,9-tetrahydro-carboline-1,5-1H-tetrazoles by a one pot Ugi-azide / Pictet-Spengler process (Figure 1b).<sup>7</sup> In 2014, we reported the synthesis of chromen-4-ones-1,5-1H-tetrazoles via the Ugi-azide reaction and *in vitro* studies of antiparasitic properties against *E. histolytica*, *G. lamblia*, and *T. vaginalis*.<sup>8</sup> Then, in 2015 we extended this work synthesizing some fluorinated analogs, which together with the previously synthesized bis-heterocycles were assayed *in vitro* against *P. aeruginosa*, *S. aureus*, *S. schenckii*, *C. albicans*, and *C. tropicalis* (Figure 1c).<sup>9</sup> Finally, just recently in 2016, we reported the synthesis of novel 3-tetrazolyl-tetrazolo[1,5-*a*]quinolines via a novel one pot Ugi-azide / SNAr / ring-chain azido-tautomerization process (Figure 1d).<sup>10</sup> As seen, the Ugi-azide reaction or its combination with further cyclization processes allows the rapid synthesis of a variety of methane-linked bis-heterocycles with potential application mainly in medicinal chemistry because 1,5-DS-T framework has been suitably combined with other heterocyclic systems, which are present in numerous bioactive products, even in drugs.

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