

**RESEARCH ARTICLE**

## Reationary ability of 3,5-Dibromo-N-Phenylanthranilic acids Derivatives

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### **ABSTRACT:**

The study of the acid-base properties of substituted N-phenylanthranilic acid is the important since, because it will allow the design of medicinal substances of this series with already known predictive properties. Therefore we have been studied the reactivity of 3,5-dibromo-N-phenylanthranilic acids has been studied. Reactivity of this isostructural group is studied in reversible conditions. The acid-base properties of 11 substituted of 3,5-dibromo-N-phenylanthranilic acids have been studied in a mixed solvent of dioxane-water (60 vol. % dioxane) at 25<sup>0</sup>C. It has been established that substitutes and their position in non-anthranilic fragment of a molecule influence on the avidity of these acids.

**KEYWORDS:** Anthranilic acid, reationary ability, acid-base properties, titration, Hammett's equation

### **INTRODUCTION:**

Derivatives of N-phenylanthranilic acid exhibit antiinflammatory, analgetic and diuretic activity<sup>[1,2,3]</sup>. These derivatives are widely applied in medicine (mefenamic acid, and its sodium salt, tolfenamic acid etc.) as effective nonsteroidal anti-inflammatory drugs. The products of these compounds' cyclization-acridines are used not only as medicines but also as analytical reagents. Therefore, the study of reactivity of 3,5-dibromo-N-phenylanthranilic acids and their derivatives is of considerable scientific and practical interest, as it allows them to optimize the synthesis and to predict pharmacological activity.

The aim of this work is to study reactivity of 3,5-dibromo-N-phenylanthranilic acids by examining their acid-base properties.

To achieve the goal the following tasks have been assigned: 1. To determine influence of substitutes structure to the avidity of 3,5-dibromo-N-phenylanthranilic acids. 2. To conduct quantitative assessment of substitutes influence in a non-anthranilic fragment of acids' molecule in terms of principles of free energies according to Hammet's equation.

### **MATERIALS AND METHODS:**

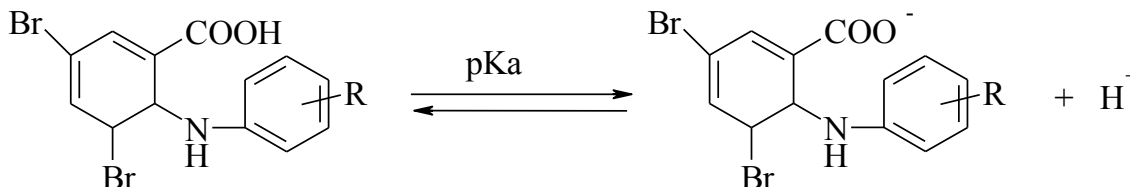
Research of acid-base equilibrium was carried out as described in technique<sup>[4]</sup>. As a titrant, the aqueous 0.05 M solution KOH was used which doesn't contain CO<sub>2</sub>. The concentration of solutions which were titrated – 0.05 M at the point of semineutralization. The potentiometric titration was performed by ionomer EV-74 with a usage of glassed (ESP-43-074) indicating electrode. By contrast, the silver chloride electrode was taken (EWP-1). The trials were three times carried out at 25<sup>0</sup>C. The accuracy of obtained results was assessed by the method of mathematical statistics of small samples (confidence level = 0.95)<sup>[4]</sup>. The mixed solvent was prepared from dioxane and freshly distilled bidistillate which is free of CO<sub>2</sub>.

**RESULTS:**

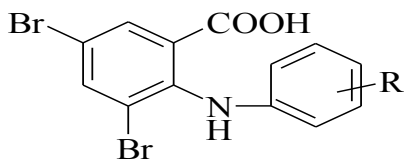
Reactivity of this isostructural group is studied in reversible conditions. The acid-base properties of 11 substituted 3,5-dibromo-N-phenylanthranilic acids

have been studied in a mixed solvent of dioxane-water (60 vol.% dioxane) at 25<sup>0</sup>C. The process is described in the equation (Scheme 1):

**Scheme 1**

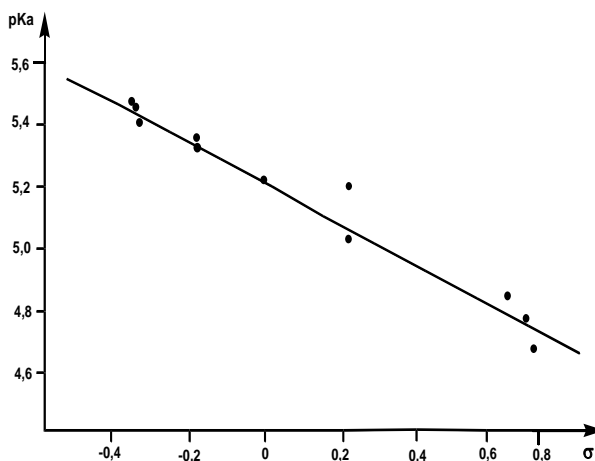


**Table 1**  
Constants of 3,5-dibromo-N-phenylanthranilic acids ions



| Compound | R                                     | pKa       |
|----------|---------------------------------------|-----------|
| 1        | H                                     | 5,26±0,03 |
| 2        | 2'-CH <sub>3</sub>                    | 5,38±0,04 |
| 3        | 4'-CH <sub>3</sub>                    | 5,35±0,01 |
| 4        | 3',4'-(CH <sub>3</sub> ) <sub>2</sub> | 5,40±0,04 |
| 5        | 4'-OCH <sub>3</sub>                   | 5,46±0,02 |
| 6        | 4'-OC <sub>2</sub> H <sub>5</sub>     | 5,44±0,02 |
| 7        | 2'-NO <sub>2</sub>                    | 4,67±0,02 |
| 8        | 3'-NO <sub>2</sub>                    | 4,74±0,03 |
| 9        | 4'-NO <sub>2</sub>                    | 4,76±0,03 |
| 10       | 4'-Br                                 | 5,06±0,01 |
| 11       | 4'-Cl                                 | 5,19±0,01 |

Data in the Table 1 reveal that 3,5-dibromo-substitutes of N-phenylanthranilic acids (1-11) are rather weak acids which avidity depends on the structure and position of substitutes in non-anthranilic fragment of a molecule. Injection of electron-accepting substitutes (-NO<sub>2</sub>, -Cl, -Br) enhances the ionization of compounds due to greater stabilization of anions. The electron-donor substitutes (CH<sub>3</sub>, -OCH<sub>3</sub>, -OC<sub>2</sub>H<sub>5</sub>) exhibit the opposite effect.



The graph of dependency pKa-f (σ) (σ-Hammett's constant) has a linear character (Fig. 1).

A quantitative estimation of substitutes influence in non-anthranilic fragment of molecule of 3,5-dibromo-N-phenylanthranilic acids (1-11) was carried out in terms of free-energy principle by the Hammett's equation [8]. Primarily, a correlation has been investigated for 3,5-dibromo-N-phenylanthranilic acid, which contain substitutes in meta- and para-position in a non-anthranilic fragment of the molecule. The correlative equation obtained (1) is statistically probable:

$$pKa = (5,26 \pm 0,03) + (0,68 \pm 0,08)\sigma \quad (1)$$

n=9    s=4,25·10<sup>-2</sup>    r=0,989

Inclusion pKa acids into correlation which contain substitutes in ortho-position in a non-anthranilic fragment of the molecule, allowed to get valuable correlative equation (2) with more improved statistical parameters:

$$pKa = (5,26 \pm 0,03) + (-0,69 \pm 0,07)\sigma \quad (2)$$

n=11    s=4,00·10<sup>-2</sup>    r=0,992

## DISCUSSIONS:

The presence of a unified correlation for ortho-, meta-, para-substitutes of 3,5-dibromo-N-phenylanthranilic acid indicates the absence of significant steric hindrance for ortho-substituted acids, as with electron-donating and with electron-accepting substitutes. The obtained equation allows predicting the acid-base properties of the other compounds of this isostructural group with a meaningful assurance level.

The analysis of parameters of correlative equation (2) indicates the low sensitivity of the reaction center (-COOH) to the effect of substitutes in the non-anthranilic fragment of the molecule of 3,5-dibromo-N-phenylanthranilic acids (reaction parameter  $\rho=0,69$ ). Eventually, it connects as with substitutes' remoteness from the reaction center, as with isolation influence of NH-group, due to the coplanarity violation of the molecule of N-phenylanthranilic acid. It ought to be noted that the reaction parameter of the examined isostructural group within boundaries of experimental deviation coincides with  $\rho$  of the other homologous groups of substitutes of N-phenylanthranilic acid, with electron-accepting substitutes in the anthranilic fragment of the molecule [5, 7, 8], that designates the unified mechanism of electronic influence of substitutes to the reaction centre.

## CONCLUSIONS:

1. The reactivity of 3,5-dibromo-N-phenylanthranilic acids has been studied in reversible conditions by examining the acid-base equilibrium in a mixed solvent of dioxane-water (60 vol.% of dioxane) at 25<sup>0</sup>C.
2. The influence of substitutes' structure and position in a non-anthranilic fragment of the molecule has been analyzed to a avidity of these acids.

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