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SYNTHESIS AND ANALYSIS OF (2Z)-4-(4-METHYLANILINO)-4-OXOBUT-2-ENOIC ACID

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p-toluidine, maleic anhydride, (2z)-4-(methylanilino)-4-oxobut-2-enoic acid, IR and NMR[1]H- spectroscopy, potentiometric titration, metrological characteristics

Abstract. *The paper identified the structure of synthesised maleic acid monoamide by physical methods of analysis. The authors have determined the solubility of maleic acid monoamide in organic solvents with different properties and dielectric constant values. The paper describes the solvent ratio allowing the analysis with the best metrological properties. The reaction between p-toluidine and maleic anhydride to form (2z)-4-(methylanilino)-4-oxobut-2-enoic acid proceeds with high yield; mass fraction of the main substance is 94.23±0.69 %.*

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Introduction

Aromatic polycarboxylic acids with additional oxygen-containing functional groups in the molecule are the most important class of chemical compounds necessary for the development of pharmaceutical, food, polymer, and other industries in Russia.

Compounds derived from maleic acid monoamide are able to reduce the action of the enzyme monoglyceridlipase. They are of great importance in many physiological processes [1]. It is possible to obtain benzylquinolcarboxylic acid from maleic acid monoamide. It blocks cells affecting the human central nervous system. Indeed, maleic acid monoamide derivatives can be used for the production of anticancer drug Carboplatin active substance. Benzothiazine derivatives obtained on the basis of monoamide are used as drugs for the treatment of diabetes mellitus and obesity [2, 3].

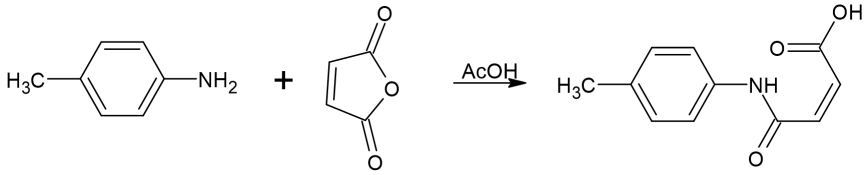
Maleic acid monoamide is also of interest as a basis for new heterocyclic compounds preparation. In combination with maleinimides they are used in the domestic polymer industry [4]. Those polymers have good chemo- and heat resistance and strength. They are used for the

production of rubber products, composite materials, and protective clothing. Currently, there is no such production in the Russian Federation; raw materials previously were supplied from Germany; nowadays they are imported from China and India.

Various methods for the synthesis of (2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid have been described in the literature [5, 6]. However, there are no data on the quantitative analysis of the target compound. Moreover, it requires additional studies.

Main body

We obtained (2Z)-4-(4-Methylanilino)-4-oxobut-2-enoic acid from the interaction of *p*-toluidine and maleic anhydride according to the procedure described in [5].



To identify the obtained compounds we used conventional physical methods of analysis: IR and ^{1}H NMR spectroscopy, melting point determination.

We determined the melting point of the obtained samples on the "Electrothermal IA" 9300 Series; the range is 188-192 °C.

We took IR spectra using a Perkin Elmer FT-IR Spectrometer ("SPECTRUM-TWO") by disturbed total internal reflection in the range 4000-400 cm^{-1} [7]. IR spectrum, ν, cm^{-1}: 3285 (NH); 1696, 1632, 1529 (C=O); 1505 (Ar-H); 970 (trans-CH=CH); 811 (1,4-substitution).

We recorded the ^{1}H NMR spectra on a Bruker MSL-300 with an operating frequency of 300 MHz. NMR data ^{1}H: 1H (δ, ppm; J, Hz): 6.24 (1H, d, J = 12.2), 6.92 (1H, d, J = 12.1), 7.45 (2H, d, J=7.7), 10.25 (1H, s), 13.31 (1H, s).

The performed research allows us to identify the obtained compound as (2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid. It is in full agreement with the results of [8]. The theoretical yield of the product according to the results of calculations was 93-97%.

The basis for the development of a new quantification technique is the consideration of reaction-analytical centres in the molecule of (2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid [9] are as follows:

1) determination of the -Ph-CH_3 radical;

2) definition of the C-N bond;

3) determination of the carbonyl group (C=O);

4) determination of the conjugated C=C bond;

5) definition of -NH- as a group containing an unshared electron pair;

6) determination of the carboxyl group (UNS).

According to literature data, dissociation constant of (2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid is 2.81±0.25. Hence, acid-base titration can be used for quantitative chemical analysis.

(2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid is insoluble in water. Therefore, we conducted the necessary study. The results are presented in Table 1.

Table 1. (2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid solubility study

Solvent	Degree of solubility	Dielectric permittivity at 25 °C
Distilled water	Not soluble	78.5
Acetone	Soluble	20.9
Isopropyl alcohol	Soluble	18.3
Triethylamine	Slightly soluble	2.4
1,4-dioxane	Slightly soluble	2.2
Chloroform	Slightly soluble	4.8
N,N-dimethylformamide	Slightly soluble	36.7

Based on the obtained data, we assume to use acetone or isopropyl alcohol for titration. They are amphiprotic solvents with close values of dielectric permittivity and autoprotholysis constants [11].

We used a standard pair for acid-base titration: glass and silver chloride electrodes. As a working solution we chose alcoholic solution of potassium hydroxide. We investigated the effect of the solvent on the confidence limits of the measurement interval by varying the ratio of the solvents chosen previously.

We performed mathematical processing of the measurement results in accordance with GOST R 8.736-2011 [12]. The series of titrations consisted of six experiments. The results are presented in Table 2.

Table 2. Effect of solvent on the confidence limits of the mass fraction measurement interval of (2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid

Solvents	Mass fraction of acid, %
Acetone	95.67±5.02
Isopropyl alcohol	84.78±2.29
Isopropyl alcohol : acetone = 1:4	96.17±3.57
Isopropyl alcohol : acetone = 4:1	92.86±1.97
Isopropyl alcohol : acetone = 3:4	92.09±3.60
Isopropyl alcohol : acetone = 4:3	94.23±0.69
Isopropyl alcohol : acetone = 1:2	95.45±1.58
Isopropyl alcohol : acetone = 2:1	89.47±3.42

According to the presented data, the smallest confidence interval of mass fraction determination results of (2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid is obtained with a mixture of solvents, isopropyl alcohol, and acetone in the ratio 4:3. These data confirm the theoretical calculations on the product yield. For comparison, in the earlier mentioned paper [5] solvents were used in the titration in the ratio 1:1; the mass fraction of acid was only 91.0%, which indicates its underestimation. The optimum ratio for titration is 4:3; the mass fraction of acid is close to the theoretically calculated value and the confidence limits of the measurement interval have the narrowest range. Thus, the accuracy of the quantitative analysis is improved.

To determine experimentally the minimum amount of the compound under study by non-aqueous potentiometric titration, a series of exact suspensions were examined, both upward and downward in mass. The solvent used was the above solvent mixture. Fig. 1 shows the experimental results. The detection limit of (2Z)-4-(4-methylanilino)-4-oxobut-2-enoic acid is 0.002 mol/dm^3.

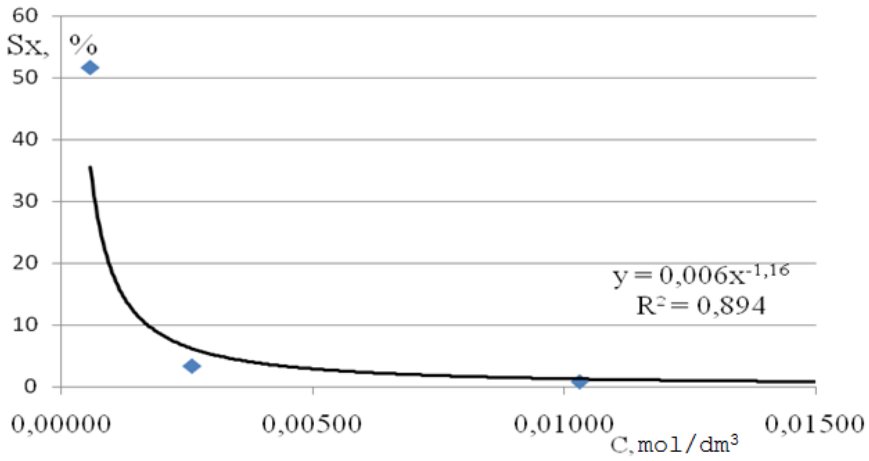


Fig. 1. Dependence of the relative standard deviation on the level of determined concentration

Conclusions

We determined the optimum isopropyl alcohol to acetone ratio of 4:3 for titration by studying the solubility of the synthesised (2z)-4-(methylanilino)-4-oxobut-2-enoic acid in various organic solvents. The mass fraction of (2z)-4-(methylanilino)-4-oxobut-2-enoic acid is (94.23±0.69)%. The data confirm the theoretical calculations on the product yield. The detection limit of the test object under the selected conditions is 0.002 mol/dm^3.

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