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Research Article

SYNTHESIS OF TWO NEW *N-BENZAMIDOMETHYL* DERIVATIVES OF TOLUENESULFONAMIDE BY DIFFERENT SYNTHETIC ROUTES

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Abstract **-** Sulfonamide compounds are among the first drugs that paved the way for the antibiotic revolution in medicine. The chemical part of sulfonamides is also present in other drugs that are not antibiotics, including thiazide diuretics, anti-diabetic drugs, COX-2 inhibitors, etc.

In order to prepare new derivatives of sulfa drugs, various synthetic procedures were performed to obtain different benzamidomethyl derivatives of toluenesulfonamide.

In two different synthetic procedures, *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide was obtained with a high yield, while in the first procedure, reactions of 4-toluenesulfonyl chloride with (benzamidomethyl)phenylamine were performed, and in the second procedure, reactions of *N*-phenyl-4-toluenesulfonamide with (benzamidomethyl)triethylammonium chloride were performed while *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide was also obtained in high yield in reactions of 4-toluenesulfonyl chloride with (benzamidomethyl)methyl amine and the other reaction between *N*-methyl-4-toluenesulfonamide with (benzamidomethyl)triethylammonium chloride.

The structures of the new compounds were confirmed and characterized by IR, ^{1}H –NMR, ^{13}C – NMR, UV spectroscopic methods and mass spectrometry.

Key words: sulfonamides, benzamidomethyl, derivatives.

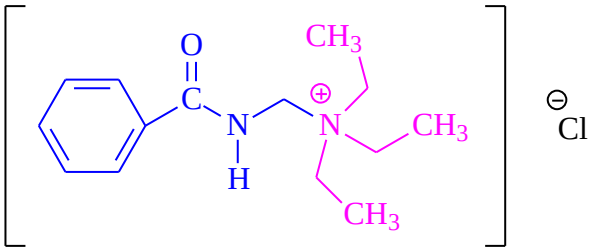
1. Introduction

There are several reasons for performing laboratory syntheses of organic molecules. In the pharmaceutical industry, new organic molecules are designed and synthesized in the hope that some of them may be useful new drugs. Complex molecules are synthesized in academic laboratories, sometimes out of a purely intellectual challenge and the mastery of new techniques. Successful modes of synthesis represent highly creative work that is sometimes described as elegant work and beautiful work [1]. In

1935, Gerhard Domagk [2] synthesized the sulfonamide called Prontosil, which inhibits the growth of streptococci. For this discovery, Domagk received the Nobel Prize for Medicine in 1939.

In their structure R can be an aliphatic, aromatic and heterocyclic group, while R_1 and R_2 can be hydrogen, alkyl, aromatic or heterocyclic group.

The problem dealt with in this scientific paper is from the field of organic synthetic chemistry. The aim of this research work was to investigate possible and most efficient synthetic routes for obtaining benzamidomethyl derivatives of toluene sulfonamide as an introduction to further research for obtaining new *N*-benzamidomethyl sulfonamide derivatives with potential biological activity. One of the synthetic routes includes benzamidomethylation reactions of toluene sulfonamide with (benzamidomethyl)triethylammonium chloride, as well as some *N*-substituted derivatives of toluene sulfonamide. This salt (Structure 1) has been shown to be highly reactive in aqueous media under relatively mild reaction conditions. The benzamidomethyl group, which directly replaces the hydrogen atom of the nucleophilic group at the substrate, is marked with a blue color, and the triethylamino group, which "leaves", is marked with a purple color.



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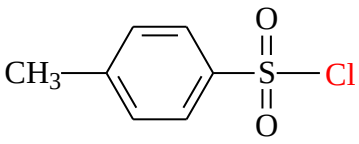
Structure 1. (Benzamidomethyl)triethylammonium chloride

The benzamidomethyl group is found in many compounds with physiological activity that show antiviral [3,4], antitumor [5], antifertility [6], antibacterial properties [7,8], acting on bacteria of the Staphylococcus aures family, antibiotic [9, 10] and other actions [11,12]. Benzamidomethyl compounds are also used as intermediates in obtaining monomers that are used to obtain synthetic resins [13].

The other synthetic route includes reactions of toluenesulfonyl chloride with benzamidomethyl amines, that is, some N-substituted derivatives of benzamidomethyl amine. Toluenesulfonyl chloride **2** is an organic compound represented by the following formula where the leaving atom is marked in red.



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Structure 2. Toluenesulfonyl chloride

2.Experimental procedure

1.1 SYNTESIS OF REAGENTS

1.1.1 *Syntesis of N- (hydroksimethyl)benzamide*

To a mixture of 17.400 g (0.1434 mol) benzamide and 2.000 g (0.0144 mol) K_2CO_3 dissolved in 36.5ml water, 36.5ml, 35% formaldehyde solution was added. The reaction mixture heated to boiling was immediately filtered while hot. The filtrate in the refrigerator crystallized after several hours. Crystals of the product were isolated by filtration under reduced pressure, washed with cold water and air dried. The *N*-(hydroxymethyl)benzamide was purified by recrystallization from water.

The melting temperature of the crystals of the product was 104°C (lit. [14] 104°C; lit. [15, 16] 104-6°C). The yield of the product was 85.3%. Infrared spectrum of *N*-(hydroxymethyl)benzamide was also recorded.

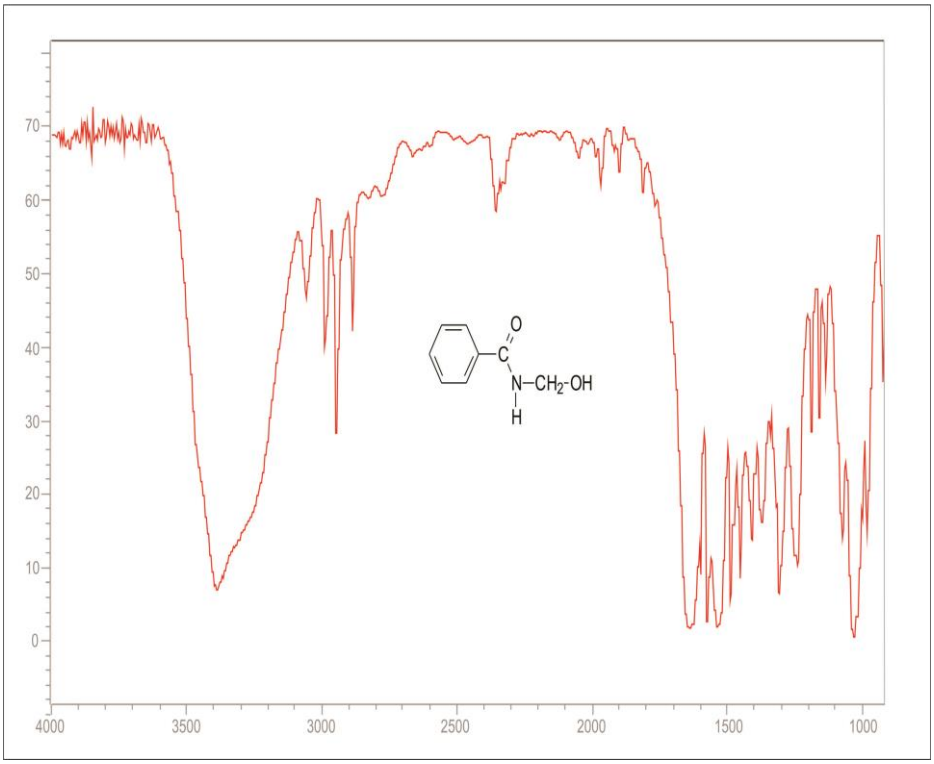


Figure 1. Infrared spectrum of *N*-(hydroxymethyl)benzamide

1.1.2 Syntesis of N- (chloromethyl)benzamide

To a suspension of 16.200 g (0.1071 mol) N–(hydroxymethyl)benzamide in 60ml CCl_4, (cooled in an ice bath) was added 21ml (0.3 mol) $SOCl_2$ in several portions.

The mixture, protected from moisture, was stirred for about 90 minutes, after which an additional 30ml was added CCl_4. After further stirring, the precipitate formed was filtered and purified by washing several times with 20ml of CCl_4.

Thus isolated *N*-(chloromethyl)benzamide in 89.8% yield was further used freshly prepared without further purification.

1.1.3 Syntesis of (benzamidomethyl)triethylammonium chloride

To a mixture of 600ml of acetone and 50.56ml (0.86 mol) of triethylamine, an acetone solution of 14.522g (0.0856 mol) of *N*-(chloromethyl)benzamide dissolved in 50ml of acetone was added with vigorous stirring. The formation of a thick suspension was immediately observed, to which an additional 100ml of acetone was added, in order to allow better mixing of the mixture. Then the mixture was filtered through a glass funnel, and the isolated product was air-dried. The yield of crude (benzamidomethyl)triethylammonium chloride, in the form of tiny white crystals, was 83.4%. Due to the large losses during the purification, this reagent was used crude in further procedures. Infrared spectrum of *N*-(hydroxymethyl)benzamide was also recorded.

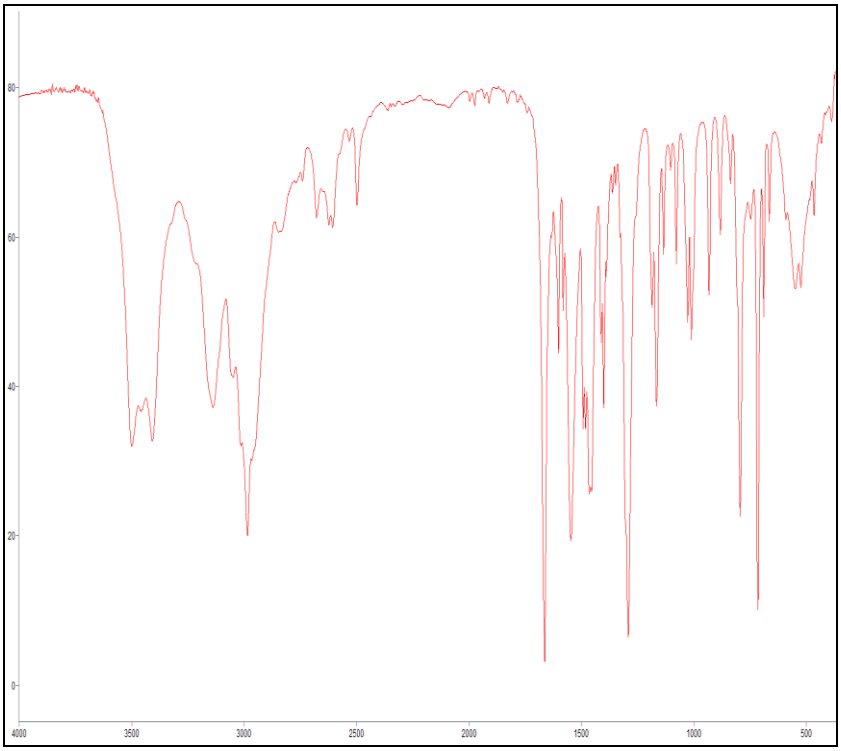


Figure 2. Infrared spectrum of (Benzamidomethyl)triethylammonium chloride

1.1.4 Syntesis of (benzamidomethyl)phenylamine

To an aqueous solution (50ml) of freshly distilled aniline (1.522g; 16.3mmol), under vigorous stirring, an aqueous solution (20ml) of (benzamidomethyl)triethylammonium chloride was added dropwise over a long period of time. The mixture was then stirred for an additional 30 minutes at room temperature. Crystals of the product were isolated by simple filtration. The yield was 90%. Purification was performed by recrystallization from toluene, whereby colorless crystals with a melting point of 116-117°C (lit. [17] 116-7°C) were obtained. The infrared spectrum data matched those from the literature [17].

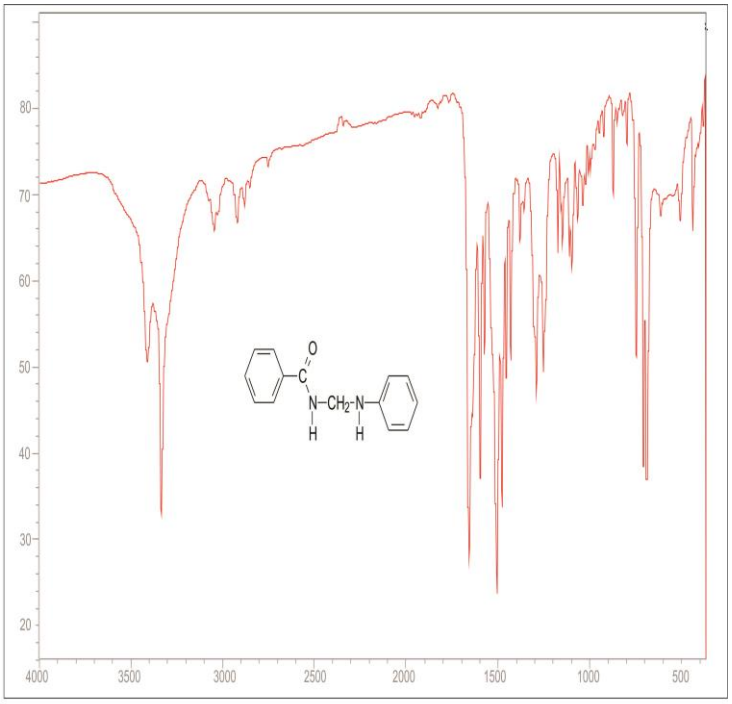


Figure 3. Infrared spectrum of (Benzamidomethyl)phenylamine

1.1.5 Syntesis of benzamidomethyl (benzamidomethyl)methylamine

To 60ml of a 33% ethanolic solution of methylamine (14.960g; 48.1mmol) was added with vigorous stirring a solution of (4.013g; 14.8mmol) (benzamidomethyl)triethylammonium chloride dissolved in 20 mL of water.

The mixture was then placed in a petri dish to evaporate the solvent. After half of the solvent was evaporated, 300mg of Na_2CO_3 was added to this mixture to leave no methylammoniumhydrochloride, but to give NaCl and to evaporate all excess methylamine. The next day, in the petri dish when everything evaporated, oil droplets and crystals were observed as a residue.Water was added to this mixture to precipitate the undesired di(benzamido)methyl amine which was removed by filtration.

In further reactions, this reagent was used as an aqueous solution without further purification.

1.1.6 Syntesis of N–phenyl-4-toluensulfonamide

In an aqueous solution of freshly distilled aniline (2.45g; 26.3mmol), well-powdered crystals of toluene sulfonyl chloride (1.672g; 8.77mmol) were added with a spatula.

The suspension was stirred for 4 hours. Thereby, the crystals of the product were created, which were filterable under vacuum. The melting point of the product was 103 °C (lit. [18] 103 °C).

2.1 SYNTESIS OF NEW COMPOUNDS

2.1.1 Syntesis of N-benzamidomethyl-N-phenyl-4-toluenesulfonamide

Method A:

A mixture of 2.308g (10.2 mmol) of (benzamidomethyl)phenylamine and 1.944g (10.2 mmol) of toluenesulfonyl chloride, 30ml of dichloromethane, and 2-3 drops of triethylamine was refluxed for about 2.5h, and then all the dichloromethane was allowed to evaporate. The isolated white crystals of the product were purified by recrystallization from ethanol. The melting point of the crystals was 167-169 °C. And the yield was 82.1%.

Method B:

To a solution of 1.42g (5.7mmol) of *N*-phenyltoluenesulfonamide in 50ml of ethanol was added a solution of 1.9435g (7.1mmol) of (benzamidomethyl)triethylammonium chloride in 10ml of water. After intensive stirring for 4 hours, colorless crystals of the product were formed which were collected by filtration under reduced pressure. The yield of the air-dried crude product was 79.8% with a melting point of 165–167°C. Recrystallization was performed with ethanol. Pure N-benzamidomethyl-N-phenyl-4-toluenesulfonamide was in the form of white fine crystals with a melting point of 167–169 °C. The yield after recrystallization was ~77.7%.

The infrared, ultraviolet, NMR and mass spectra of the new compound were recorded.

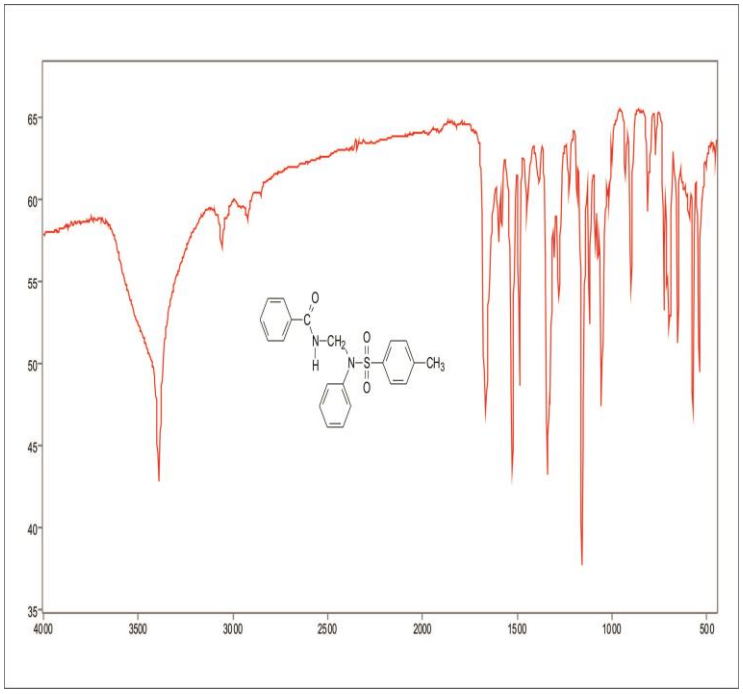


Figure 4. Infrared spectrum of N-benzamidomethyl-N-phenyl-4-toluenesulfonamide

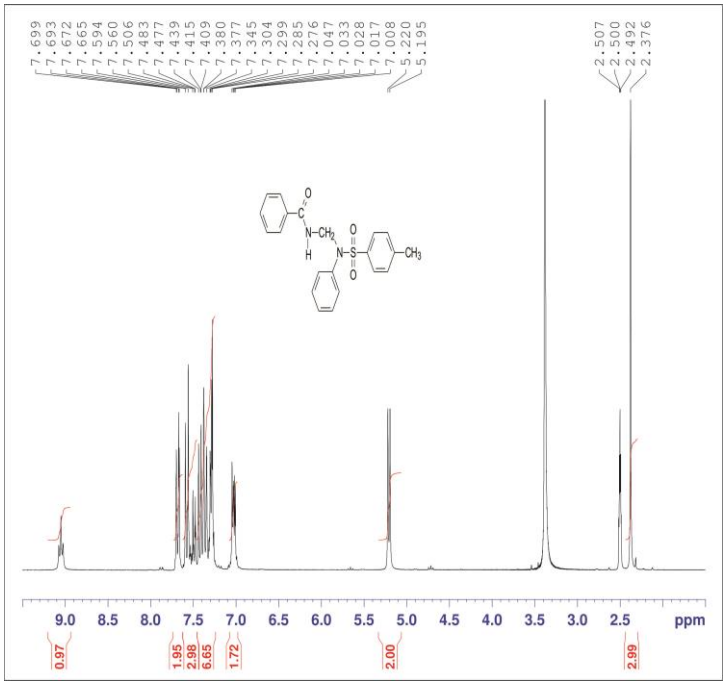


Figure 5. ^{1}H–NMR spectrum of *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide

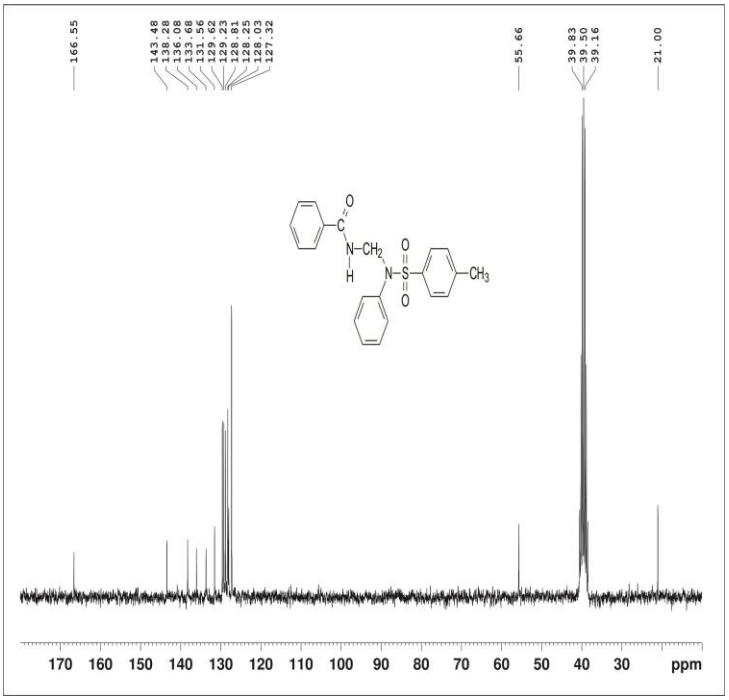


Figure 6. ^{13}CNMR spectrum of *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide

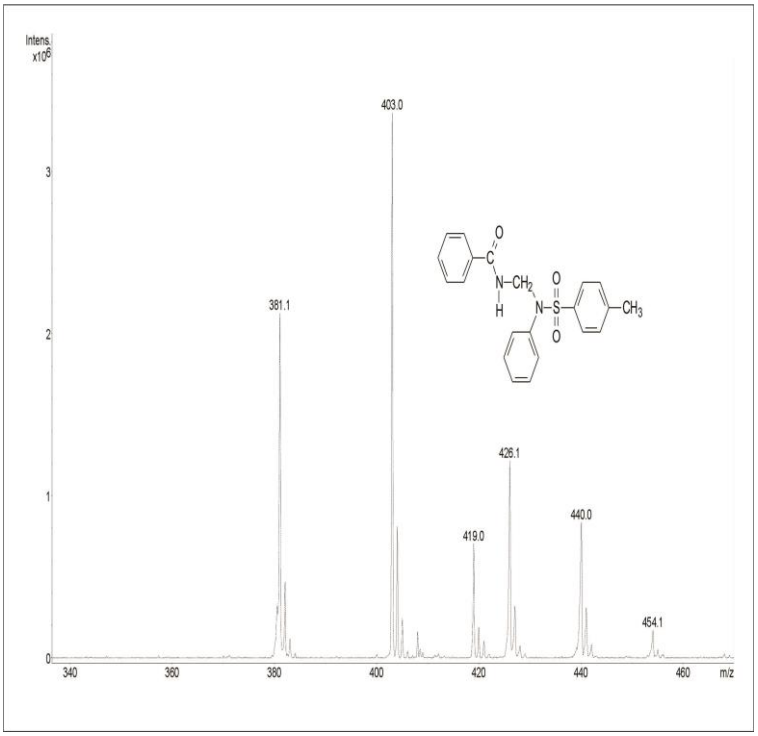


Figure 7. MS (ESI pos) spectrum of *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide

2.1.2 Syntesis of N-benzamidomethyl-N-methyl-4-toluenesulfonamide

Method A:

To a concentrated aqueous solution of (benzamidomethyl)methylamine (~2.803g; 14.0 mmol) synthesized previously was added with a spatula finely powdered toluenesulfonyl chloride (2.878g; 15.1mmol) and 200mg of Na_2CO_3. After half an hour, the suspension started to change color from gray to white, and after 3 hours all the crystals were white. Crystals from the product were filtered off and recrystallized with ethanol. Pure *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide was in the form of small colorless crystals with a melting point of 127–129°C. The yield after recrystallization was ~77.2%.

Method B:

To a solution of 0.953g (5.1mmol) of methyltoluenesulfonamide dissolved in 30 ml of ethanol was added a solution of 1.706g(6.3mmol) of (benzamidomethyl)triethylammonium chloride dissolved in 5-6 ml of water.

Upon vigorous stirring, the appearance of crystals in the solution was observed. After 3-4 hours the crystals were collected by filtration under reduced pressure. The yield of the air-dried crude product was 79.2% with a melting point of 128–129°C. Recrystallization was performed with ethanol.

Pure *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide was in the form of small colorless crystals with a melting point of 127–129°C. The yield after recrystallization was ~75.0%.

Also the infrared, ultraviolet, NMR and mass spectra of the new compound were recorded.

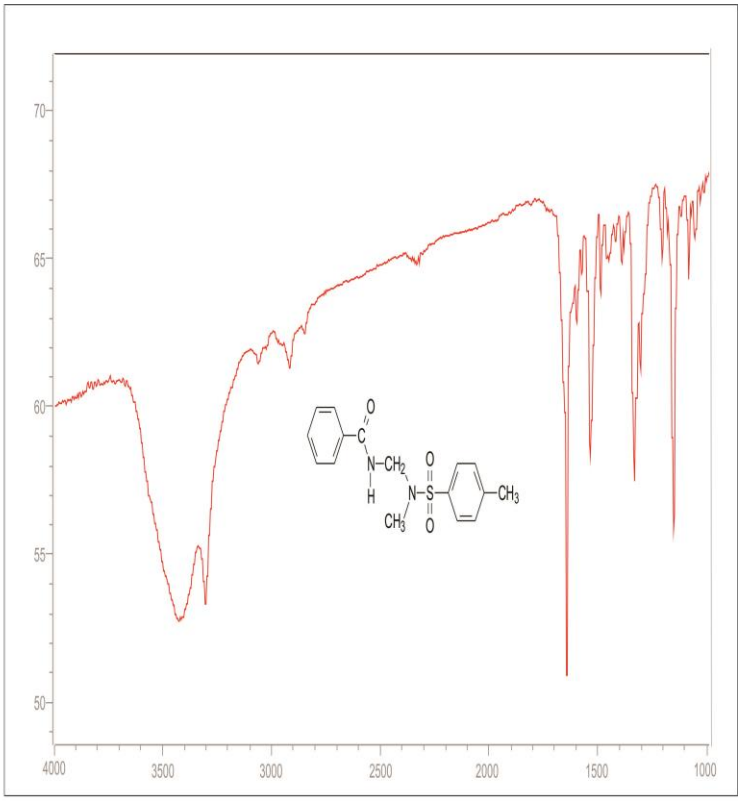


Figure 8. Infrared spectrum of *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide

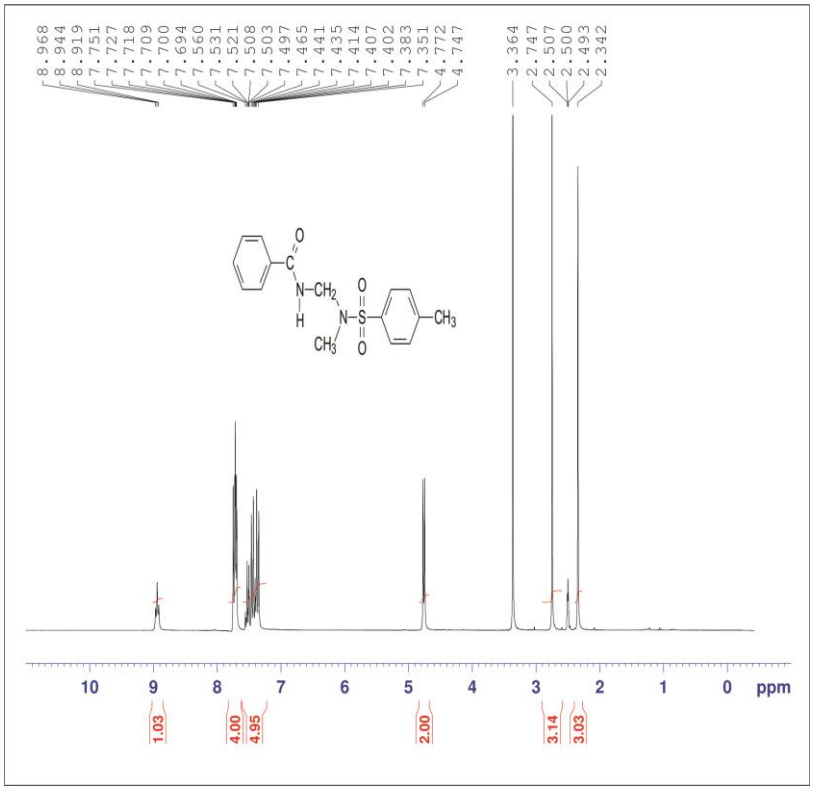


Figure 9. [1]HNMR spectrum of *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamid

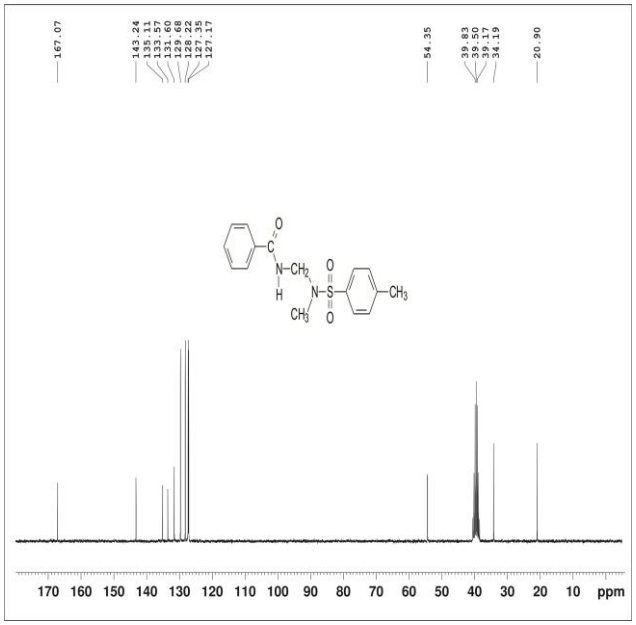


Figure 10. ^{13}CNMR spectrum of *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide

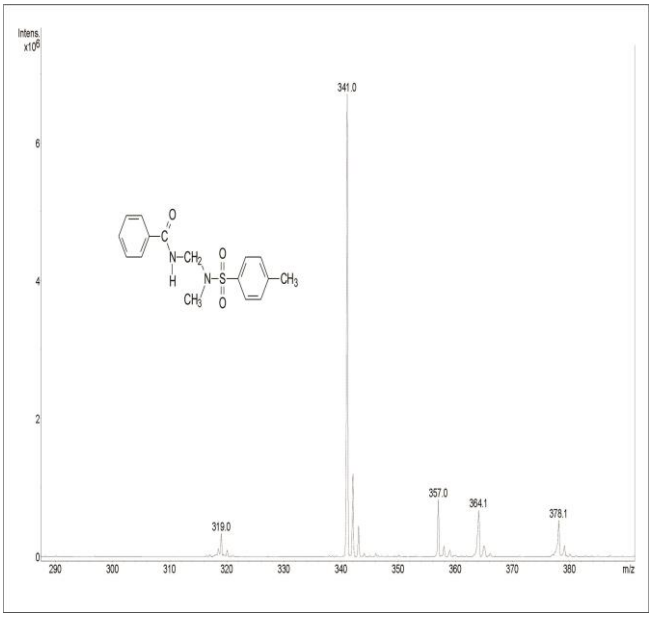


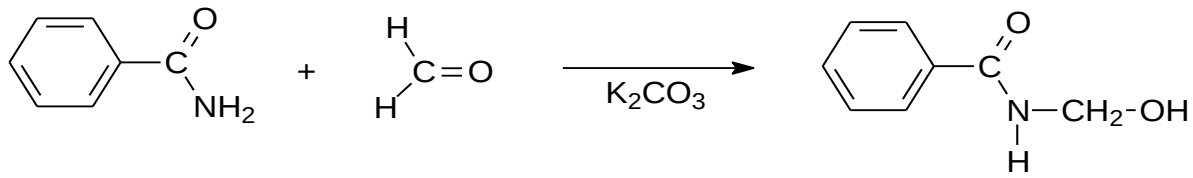
Figure 11. MS (ESI pos) spectrum of *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide

3.Results and discussion

At the beginning of this paper, the synthesis of (benzamidomethyl)triethylammonium chloride was approached. This compound was used not only as a reagent for the benzamidomethylation of toluenesulfonamides but also as a precursor to obtain the corresponding benzamidomethylamines which were further used as nucleophiles in reactions with toluenesulfonyl chloride.

Preparation of (benzamidomethyl)triethylammonium chloride

To obtain the main reagent, *N*-(hydroxymethyl)benzamide was first synthesized, in order to obtain *N*-(chloromethyl)benzamide from which (benzamidomethyl)triethylammonium chloride was obtained. The synthesis of N-(hydroxymethyl)benzamide was performed according to the method of Einhorn [19]. The benzamide was boiled in a 35% aqueous formaldehyde solution in a weak basic medium (Scheme 1) and the solution was then filtered. During cooling of the filtrate, crystals of N-(hydroxymethyl)benzamide precipitated. The yield of the product was 85.3%.

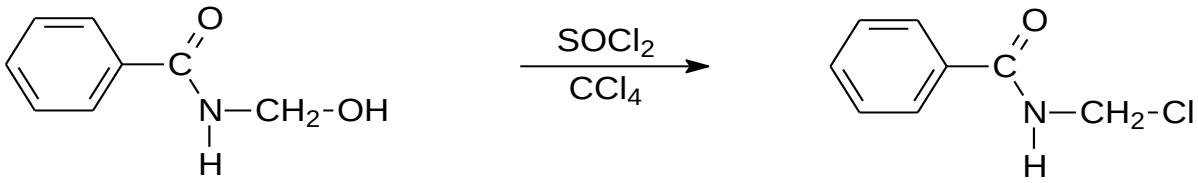


Scheme 1. Reaction to obtain N-(hydroxymethyl)benzamide

The resulting *N*-(hydroxymethyl)benzamide was recrystallized with water. Identification was performed by melting temperature and from the recorded IR spectrum (Figure 1). In the infrared spectrum in the region 3400-3250 cm^{-1} an intense broad band with a transition can be observed. This band is composed of two overlapping bands due to the O-H and N-H valence vibrations.

The band due to the Amide I vibration occurs at 1634 cm^{-1}, while at 1540 cm^{-1} is the Amide II band originating from the vibration.

There are several methods for substituting the hydroxyl group in *N*-(hydroxymethyl)benzamide. Chlorination can be performed with PCl_5 [20-22], with $SOCl_2$ [23], or with $(OCCl)_2$ [24], where complete anhydration of the medium in which the reaction takes place must be observed. Namely, to a suspension of *N*-(hydroxymethyl)benzamide in dry CCl_4, the entire required amount of $SOCl_2$ was added partially during 30 minutes (Scheme 2).

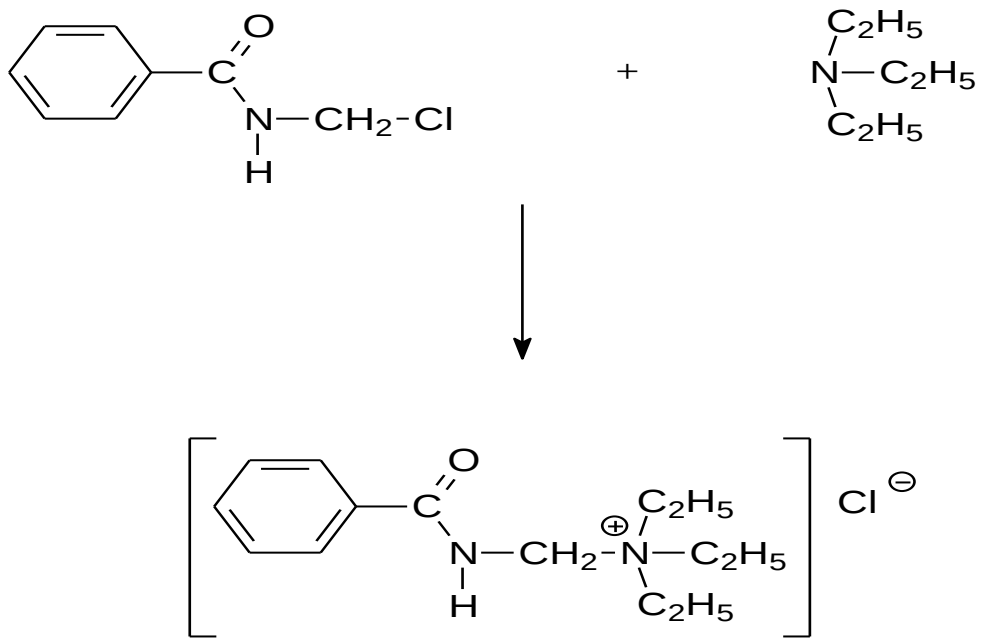


Scheme 2. Reaction to obtain *N*-(chloromethyl)benzamide

The obtained *N*-(chloromethyl)benzamide is a colorless crystalline substance and due to its high reactivity, it was not recrystallized and was used freshly prepared in further syntheses. The reagent

(benzamidomethyl)triethylammonium chloride that we used in our experiments was obtained in a simple way (Scheme 3).

An acetone solution of freshly prepared *N*-(chloromethyl)benzamide was suddenly added to a solution of triethylamine in acetone, and the formation of a white precipitate from the product was immediately visible. During the synthesis, 3 times the amount of triethylamine was used in relation to *N*-(chloromethyl)benzamide, and the mixture was vigorously stirred for a period of 30 minutes. Due to the large losses during recrystallization, this reagent was used without purification in further syntheses. Identification of the product was performed through the data obtained from the recorded infrared spectra.



Scheme 3. Reaction to obtain (benzamidomethyl)triethylammonium chloride

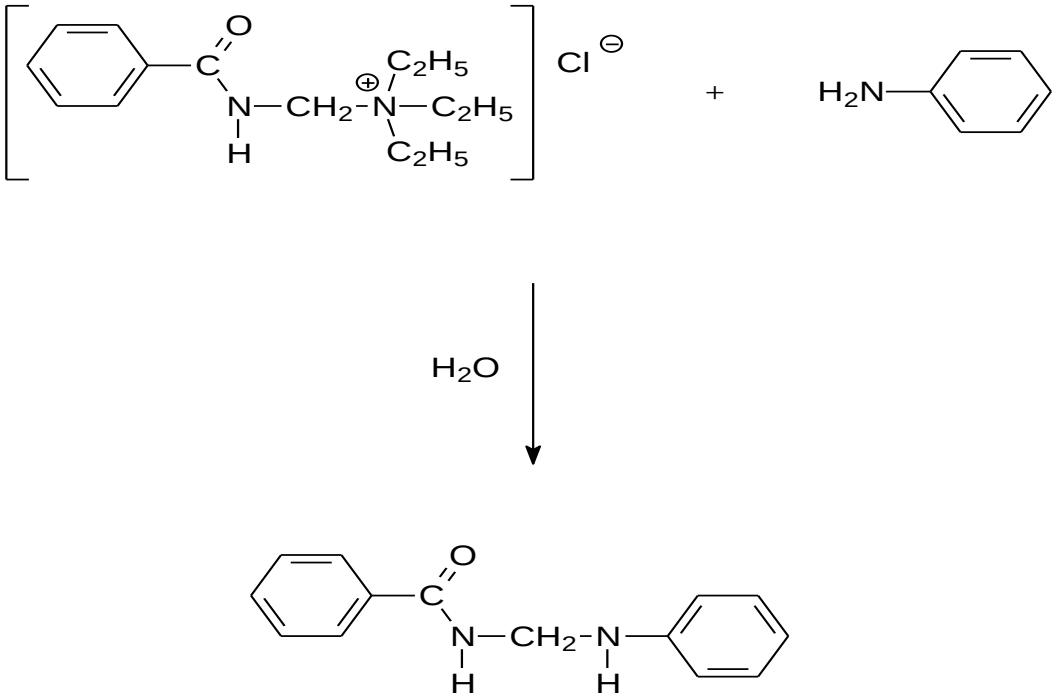
In the infrared spectrum of (benzamidomethyl)triethylammonium chloride (Figure 2), intense bands from 3140 to 2840 cm^{-1} can be observed. These bands are due to C-H valence vibrations from the CH_2CH_3 groups present. Amide I and Amide II vibrations give bands of strong intensity and are observed at 1662 cm^{-1} and 1546 cm^{-1}, respectively.

Preparation of *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide

N-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide was obtained in two different synthetic procedures. In the first procedure, reactions of 4-toluenesulfonyl chloride with (benzamidomethyl)phenylamine were performed, and in the second procedure, reactions of *N*-phenyl-4-toluenesulfonamide with (benzamidomethyl)triethylammonium chloride were performed.

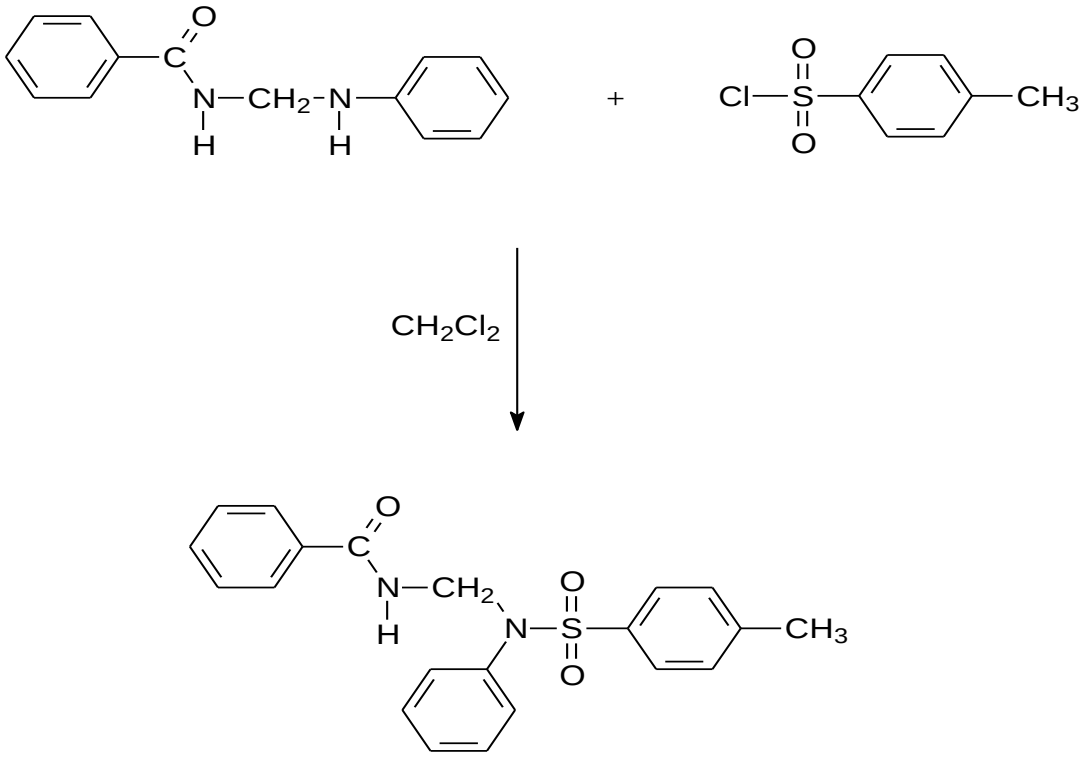
Reactions of 4-toluenesulfonyl chloride with (benzamidomethyl)phenylamine

In order to obtain (benzamidomethyl)phenylamine, a dilute aqueous solution of (benzamidomethyl)triethylammonium chloride was added (dropwise) to a concentrated aqueous solution of aniline over a long period of time [17]. The amount of aniline was three times greater than that of (benzamidomethyl)triethylammonium chloride (Scheme 4). The product was identified by the melting temperature and recorded IR spectrum (Figure 4).



Scheme 4. Reaction to obtain (benzamidomethyl)phenylamine

The (benzamidomethyl)phenyl amine thus obtained was dissolved in dichloromethane and to this solution was added toluenesulfonyl chloride. To this mixture, under vigorous stirring, 3-4 drops of triethylamine were added. The reaction mixture was refluxed for about 2,5 hours and then left at room temperature to evaporate all the dichloromethane. Colorless crystals of the product *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide were purified by recrystallization from ethanol. The melting point of the product crystals was 167-169 °C. The yield of the product was 82.1%.



Scheme 5. Reaction of (benzamidomethyl)phenylamine and toluenesulfonyl chloride

In the IR spectrum of *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide, a band of strong intensity at 3392 cm^{-1} from the valence vibration of the NH bond was observed, as well as a band of strong intensity from the Amide I vibration at 1670 cm^{-1} and Amide II vibration at 1529 cm^{-1}, as well as a band at 1160 cm^{-1} from the S=O bond (Figure 4).

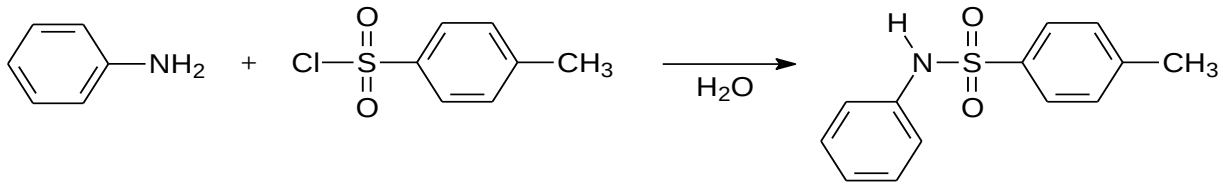
In the ^{1}H–NMR spectrum, a triplet at 9.05 ppm from the hydrogen atom of the NH group was recorded, multiple signals from 14 aromatic hydrogen atoms in the region of 7.70 ppm – 7.01 ppm, a doublet at 5.20 ppm from the two protons of CH_2, and at 2.38 ppm a singlet occurs from the three protons of the CH_3 group (Figure 5).

In the ^{13}C–NMR spectrum, bands were observed from the carbon atom of the carbonyl group at 166.5 ppm, a band at 55.7 ppm from the C atom of the CH_2 group, and a band from the C atoms of the CH_3 group in the region of 21.0 ppm (Figure 6) .

In the ESI pos mass spectrum, the molecular ion $[M+H]^+$ was detected at 381.1.0 m/z (Figure 7). This was an additional confirmation of the structure of the product considering the molecular mass of *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide which is 380.5 g/mol.

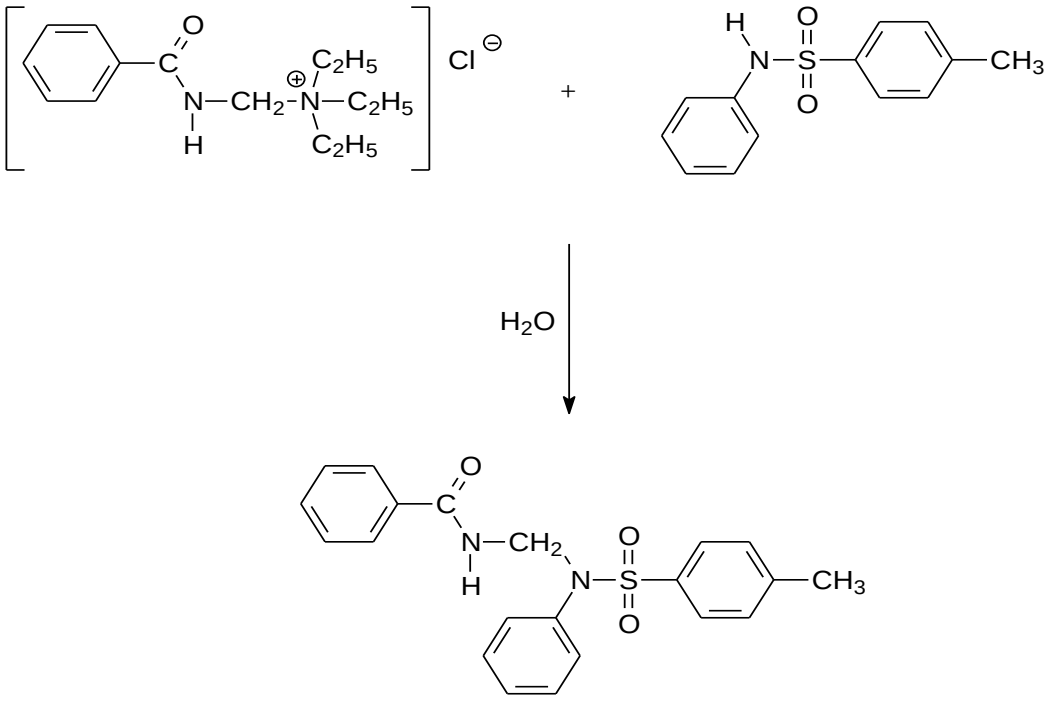
Reactions of *N*-phenyl-4-toluenesulfonamide with (benzamidomethyl)triethylammonium chloride

The nucleophile, *N*-phenyltoluenesulfonamide, required to obtain *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide was obtained in a reaction carried out in aqueous medium [22]. Toluenesulfonyl chloride was added to an aqueous solution of aniline in a 1:2 volume ratio under vigorous stirring (Scheme 6). The formation of crystals from the product was observed, which was identified through the melting temperature [18].



Scheme 6. Reaction to obtain *N*-phenyl-4-toluenesulfonamide

Further, the resulting *N*-phenyl-4-toluenesulfonamide was dissolved in ethanol. To this solution, an aqueous solution of (benzamidomethyl)triethylammonium chloride was added (Scheme 7). After vigorous stirring (~2h) at room temperature, the newly formed colorless crystals were separated by filtration under reduced pressure. Pure *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide was in the form of colorless small crystals with a melting point of 167–169°C. The yield after recrystallization was ~77.7%. Identification was also performed through the recorded IR spectrum.



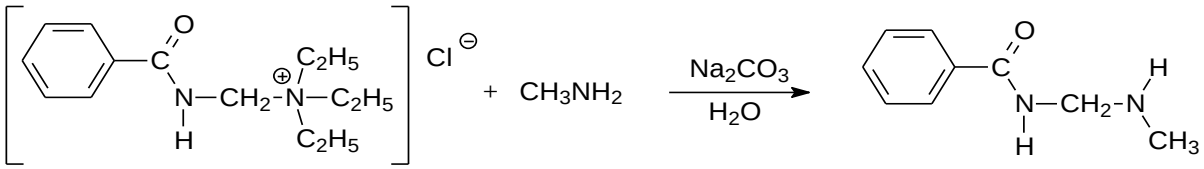
Scheme 7. Reaction of phenyltoluenesulfonamide and (benzamidomethyl)triethylammonium chloride

Preparation of *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide

Like the previous three derivatives, *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide was obtained in two different synthetic procedures. In the first procedure, reactions of 4-toluenesulfonyl chloride with (benzamidomethyl)methylamine were performed, and in the second procedure, reactions of *N*-methyl-4-toluenesulfonamide with (benzamidomethyl)triethylammonium chloride were performed.

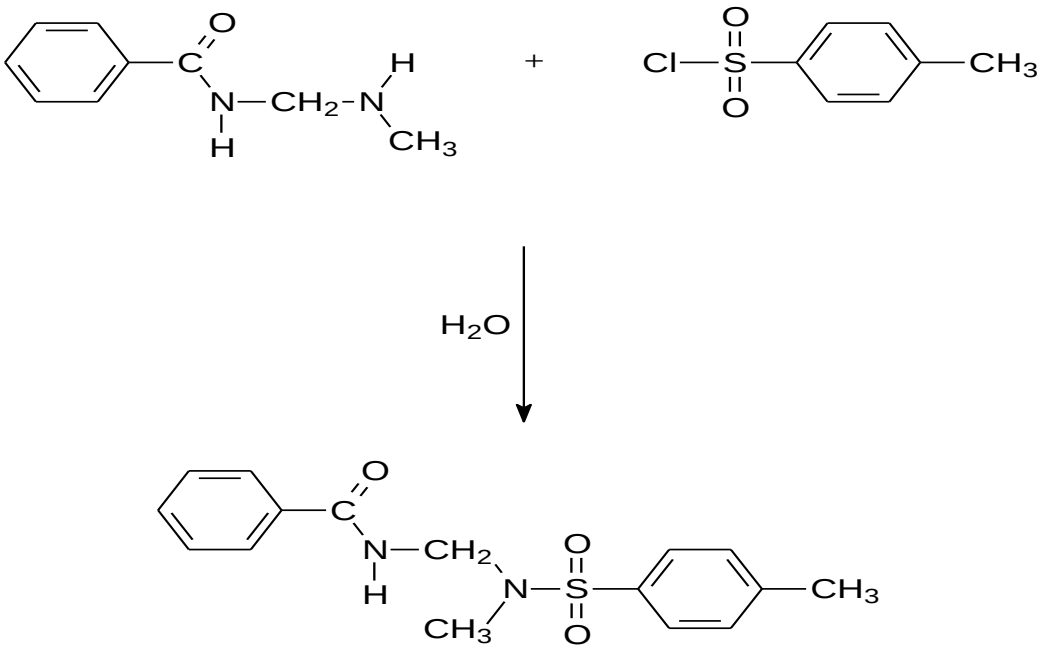
Reactions of 4-toluenesulfonyl chloride with (benzamidomethyl)methylamine

During the reaction of (benzamidomethyl)triethylammonium chloride and an ethanolic solution of methyl amine, the (benzamidomethyl)methylamine needed in the further procedure was obtained. A dilute aqueous solution of (benzamidomethyl)triethylammonium chloride was added to a concentrated ethanolic solution of methylamine with vigorous stirring. After stirring for 30 minutes, Na_2CO_3 was added to the mixture to prevent the formation of methylammoniumhydrochloride (Scheme 8). Then, the mixture was left at room temperature until all the solvent had evaporated.



Scheme 8. Preparation of (benzamidomethyl)methylamine

The next day, after evaporation of the solvent, a mixture of oily droplets and crystals was observed. Water was added to this mixture to remove unwanted di(benzamido)methylamine as colorless crystals. The solution was filtered and the filtrate with (benzamidomethyl)methylamine was further used without further purification. To the filtrate obtained earlier, an aqueous solution of toluenesulfonyl chloride and Na_2CO_3 was added (Scheme 9). After half an hour, the suspension started to change color from gray to white, and after 3 hours all the crystals were white. Crystals of the product were recrystallized from ethanol. Pure *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide was in the form of small colorless crystals with a melting point of 127–129 °C. The yield after recrystallization was ~77.2%.



Scheme 9. Reaction of (benzamidomethyl)methylamine and 4-toluenesulfonyl chloride

In the IR spectrum of *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide, a band at 3312 cm^{-1} from the valence vibrations of the NH bond was observed, as well as an intense band from the Amide I vibration at 1647 cm^{-1} and the Amide II vibration at 1541 cm^{-1} as well as the band at 1158 cm^{-1} from the S=O bond. (Figure 8).

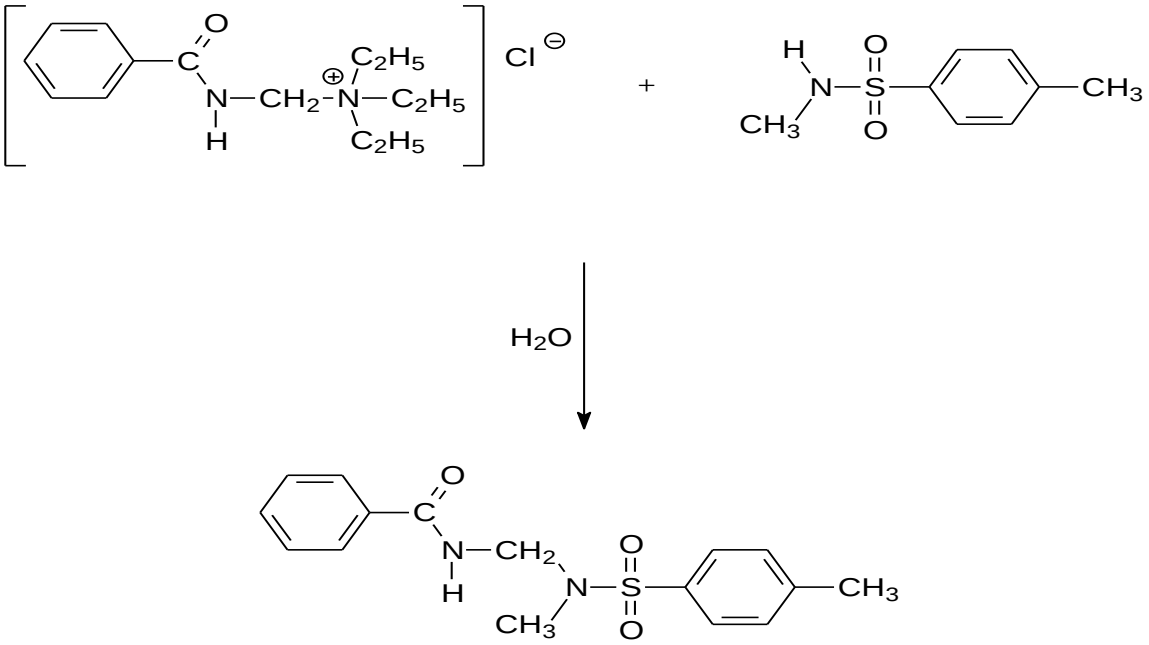
Concrete proof of the dialkyl nature of the product was given by the ^{1}H–NMR spectrum (Figure 9). A triplet at 8.94 ppm from the hydrogen atom of the NH group, multiple signals from the 9 aromatic hydrogen atoms in the region of 7.75 ppm – 7.35 ppm as well as a doublet at 4.76 ppm from the hydrogen atoms of both $NHCH_2$ were recorded. groups. A singlet occurs at 2.75 ppm from the three hydrogen atoms of the N-CH_3 group and at 2.34 ppm a singlet also occurs from the three hydrogen atoms of the CH_3 group. In the ^{13}C–NMR spectrum (Figure 10) bands of carbon atoms of C=O in the region of 167 ppm, CH_2 group at 54.3 ppm, N-CH_3 at 34.2 ppm and CH_3 group at 20.9 ppm were identified, as and 8 bands from the aromatic carbon atoms in the region of 143.2 ppm – 127.2 ppm.

In the mass spectrum and ESI pos (Figure 11) the molecular ion $[M+H]^+$ at 341.0 m/z was observed. Considering the molecular mass of the product 341.3 g/mol this was another confirmation of the expected structure.

Reactions of *N*-methyl-4-toluenesulfonamide with (benzamidomethyl)triethylammonium chloride

To a solution of *N*-methyltoluenesulfonamide dissolved in ethanol, a solution of (benzamidomethyl)triethylammonium chloride in water was added (Scheme 10).

Upon vigorous stirring, the appearance of crystals in the solution was observed. The crystals were collected by filtration under reduced pressure. Purification was performed with ethanol. Pure *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide was in the form of small colorless crystals with a melting point of 127–129°C. The yield after recrystallization was ~79.0%. Identification was performed through melting temperature as well as infrared spectrum data.



Scheme 10. Reaction of methyltoluenesulfonamide and (benzamidomethyl)triethylammonium chloride

UV spectroscopic characteristics of the obtained compounds

In this scientific paper, the UV spectra of the two new *N*-benzamidomethyl derivatives of 4-toluenesulfonamide were also recorded. For an appropriate comparison of the spectroscopic characteristics of the synthesized compounds, in their UV spectra instead of absorbance, values for the molar absorption coefficient ε/mol-1 dm3 cm-1 are given on the ordinate (Figure 12)

—— *N*-benzamidomethyl-*N*-methyl-4-toluenesulfonamide
—— *N*-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide
—— 4- toluenesulfonamide

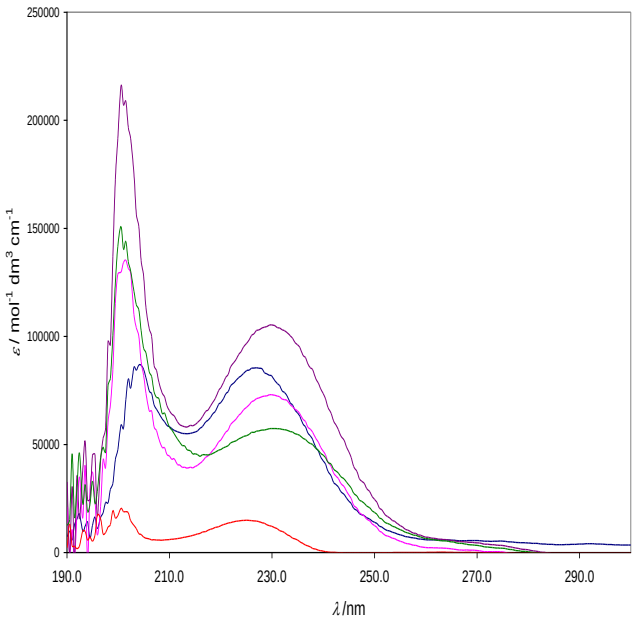


Figure 12. Dependence of molar absorption coefficient on wavelength in TSA and synthesized compounds

The following table gives the corresponding characteristics for absorption bands, ie. absorption maxima and the logarithmic values of the molar absorption coefficients.

Table 1. Position of the absorption bands in the UV spectra of the synthesized compounds

Compound	λ_{max} /nm			
	λ_{max} /nm	log {ε}*	λ_{max} /nm	log {ε}*
benzamide[26]	194	4,42	227	3,91
4- toluenesulfonamide	200,5	4,31	225	4,18
N-benzamidomethyl-*N*-methyl-4-toluenesulfonamide	201,5	5,13	230	4,86
N-benzamidomethyl-*N*-phenyl-4-toluenesulfonamide	200,5	5,18	230,5	4,76

* Values of log [ε/(mol-1 dm3 cm-1)] are determined in ethanol

If we make a comparison in relation to the spectrum of 4-toluenesulfonamide, it is noticeable that the absorption maxima of the two bands in the obtained benzamidomethyl derivatives are shifted bathochromically, accompanied by a strongly expressed hyperchromic effect (increase in absorption).

At the same time, the position of the absorption maxima (Table 1) is close to that of benzamide, taking into account the fact that mono and disubstituted benzene derivatives absorb at higher wavelengths than benzene.

4.Conclusion

The problem dealt with in this scientific paper is from the field of organic synthetic chemistry. The aim of this research work was to investigate the most efficient synthetic routes for obtaining benzamidomethyl derivatives of toluenesulfonamide as an introduction to further research for obtaining new *N*-benzamidomethyl sulfonamide derivatives with potential biological activity.

One of the synthetic procedures included benzamidomethylation reactions of 4-toluenesulfonamide with (benzamidomethyl)triethylammonium chloride.

For this purpose, at the beginning, (benzamidomethyl)triethylammonium chloride was synthesized, which has been used as a reagent for many years in the laboratory of the Institute of Organic Chemistry of the Institute of Chemistry at the Faculty of Science and Mathematics in Skopje

The other synthetic procedure involved reactions of 4-toluenesulfonyl chlorides with (benzamidomethyl)amine. Toluenesulfonyl chloride was purchased commercially, while benzamidomethyl amines were synthesized according to already known procedures. The following can be concluded from the results obtained during the preparation of this research work:

- In the reaction of *N*-methyl-4-toluenesulfonamide with (benzamidomethyl)triethyl-ammonium chloride according to one synthetic procedure and the reaction of toluenesulfonyl chloride with (benzamidomethyl)methylamine according to another synthetic procedure, the following was obtained:
  - ✓ ***N*–benzamidomethyl-*N*-methyl-4- toluenesulfonamide**
- In the reaction of *N*-phenyl-4-toluenesulfonamide with (benzamidomethyl)triethyl-ammonium chloride according to one synthetic procedure and the reaction of toluenesulfonyl chloride with (benzamidomethyl)phenylamine according to another synthetic procedure, the following was obtained:
  - ✓ ***N*–benzamidomethyl-*N*-phenyl-4- toluenesulfonamide**
- The structure of the obtained compounds was confirmed and characterized by the data obtained from their FTIR, ^{1}H–NMR, ^{13}C–NMR, UV and mass spectra.
- Within the framework of this research work, 2 new *N*-benzamidomethyl derivatives of 4-toluenesulfonamide were synthesized following different synthetic procedures, for which there were no previously known literature data.
- The results and conclusions obtained in this research work will be a roadmap for future research to obtain new benzamidomethyl derivatives of sulfonamides with potential biological activity.

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