ХИМИЧЕСКИЕ НАУКИ

NEW ESTERODIOL WITH IMIDAZOQUINAZOLINE RING

Szyszkowska A.

Rzeszow University od Technology,
Rzeszów, Poland

Zarzyka I.

Rzeszow University od Technology,
Rzeszów, Poland

ABSTRACT

The results of the new esterodiol synthesis obtained in reactions of 2,6-bis-(ethoxycarbonylmethyl)-1-phenylimidazo[1,5-c]quinazoline-3,5-dione with excess of ethylene glycol have been presented. The product was isolated at high yield and characterised by spectral methods (IR, ^{1}H-and ^{13}C-NMR). 2,6-bis-[(2-hydroxy-ethoxy)carbonylmethyl)]-1-phenylimidazo[1,5-c]quinazoline-3,5-dione can be used as a biological active compound.

KEYWORDS

imidazoquinazoline, transesterification, ethylene glycol, diol

INTRODUCTION

Imidazoquinoline and imidazoquinazoline derivatives have interesting biological properties [1-3]. Derivatives of imidazo[1,5-c]quinazoline-3,5-dione, obtained during reaction of 3-aminoquinolinediones with urea as a result of rearrangement [4, 5], can also have biological activity. The scheme of the mentioned rearrangement is shown in Figure 1.

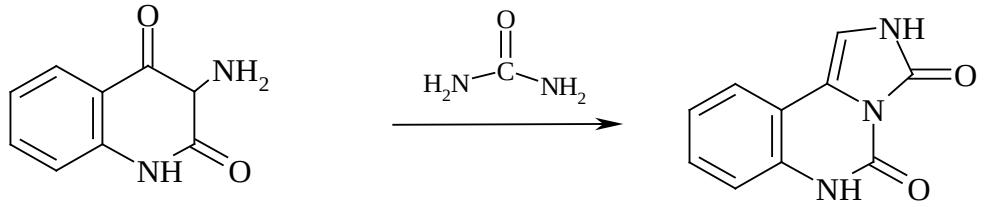

Figure 1 – Synthesis scheme of 2H,6H-imidazo[1,5-c]quinazoline-3,5-dione from 3-amine-1H,3H-quinoline-2,4-dione

Unfortunately, these derivatives are sparingly soluble and because of that fact their application is difficult and even impossible. Therefore, new derivatives with imidazo[1,5-c]quinazoline-3,5-dione ring are needed which will have better solubility. One of the solutions is obtaining hydroxyl derivatives. This work refers to synthesis hydroxyl derivative of 1-phenyl-2H,6H-imidazo[1,5-c]quinazoline-3,5-dione and its spectral characterization.

RESULTS AND DISCUSSION

New esterodiol was formed in reaction of 2,6-bis(ethoxycarbonylmethyl)-1-phenylimidazo[1,5-c]quinazoline-3,5-dione with an excess of ethylene glycol in the presence of zinc acetate, which was shown in Figure 2. Obtained esterodiol is readily soluble in chloroform.

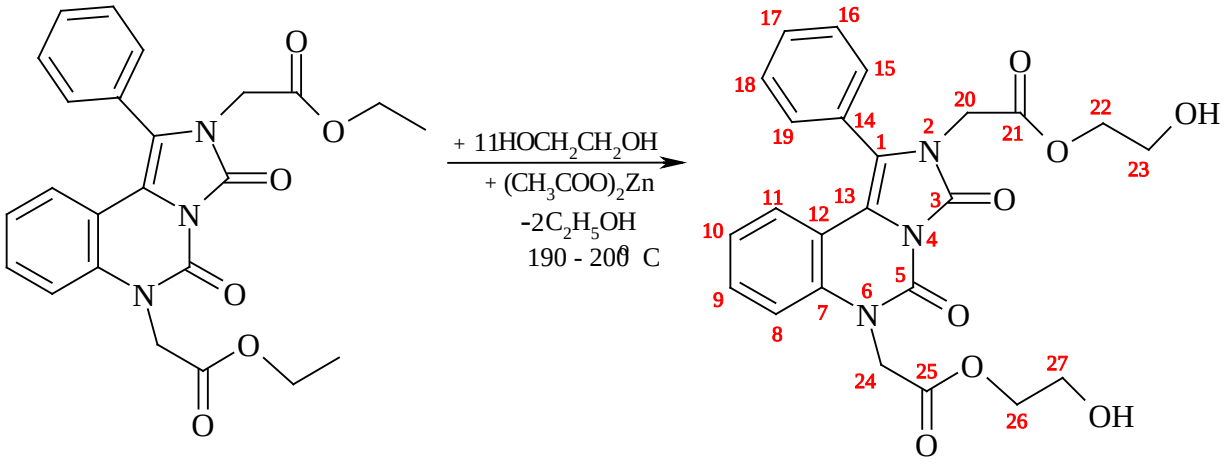

Figure 2 – Synthesis scheme of 2,6-bis[(2-hydroxyethoxy)carbonylmethyl]-1-phenyl-imidazo[1,5-c]quinazoline-3,5-dione

2,6-bis(methoxycarbonylmethyl)-1-phenylimidazo[1,5-c]quinazoline-3,5-dione was obtained with good yield (70 %). Its melting point is 99°C. Spectral analysis confirmed the structure of the new esterodiol. In the ^{1}H-NMR spectrum of the starting ester (Fig. 3), two triplets at the chemical shift 1.06 and 1.25 ppm are observed. They originated from protons from methyl groups (C23) and (C27), respectively. The protons of the methylene groups (C22) or (C26) of ethoxy group giving two quartets at 4.05 and 4.20 ppm. In turn, the protons of the methyl groups attached directly to the nitrogen atoms (N2 and N6) appears in the form of two singlets at the chemical shift of 4.25 and 4.9 ppm.

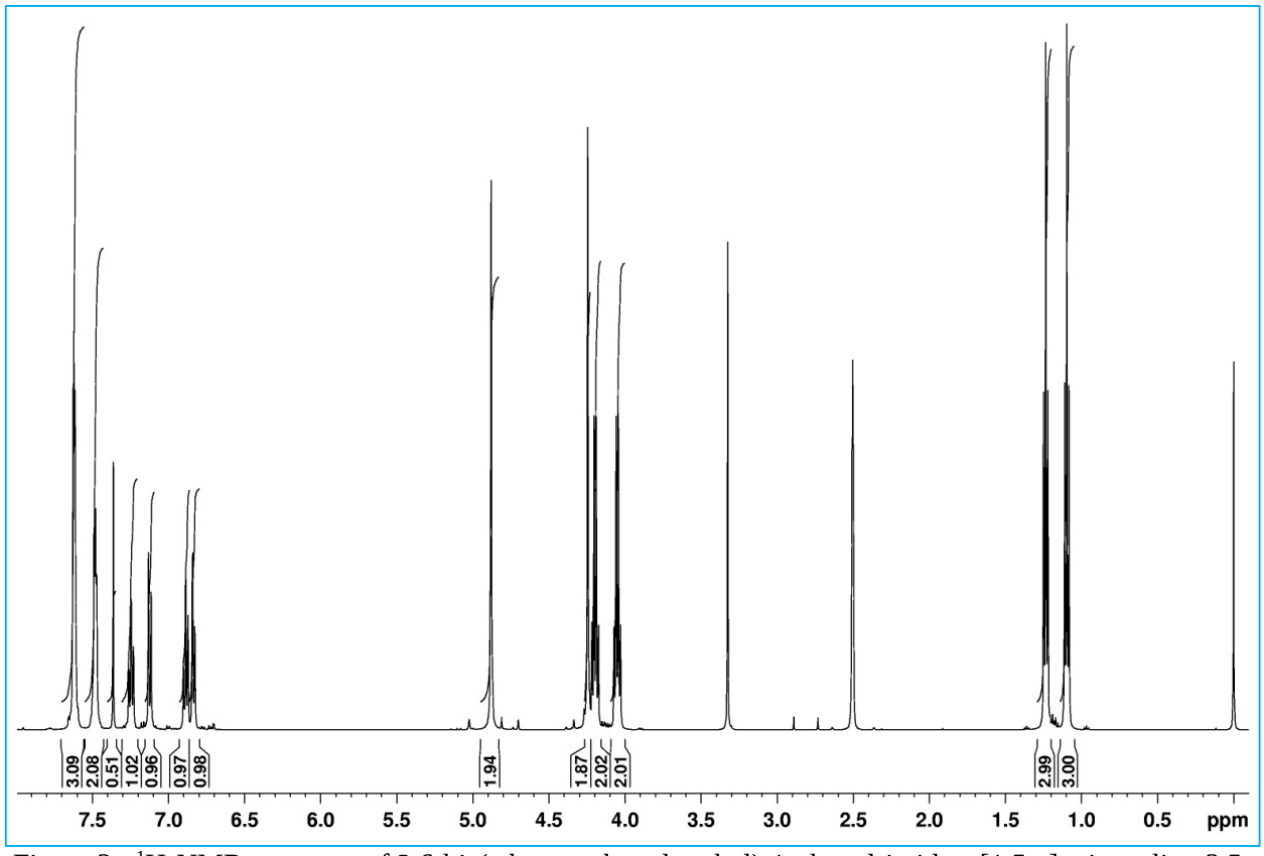

Figure 3 - ^{1}H-NMR spectrum of 2,6-bis(ethoxycarbonylmethyl)-1-phenyl-imidazo[1,5-c]quinazoline-3,5-dione

In the ^{1}H-NMR spectrum of 2,6-bis(ethoxycarbonylmethyl)-1-phenylimidazo-[1,5-c]quinazoline-3,5-dione (Fig. 4), we observed significant changes. Triplets at the chemical shift 1.06 and 1.25 ppm disappeared and we can see new two triplets at 3.50 and 3.65 ppm from methylene groups linked to hydroxyl groups (CH_2-OH – C23 and C27, respectively). In addition, there are signals of

hydroxyl groups at the chemical shift of 4.8 and 4.9 ppm. The second one is overlapped the signal of a methylene group linked to nitrogen atom number 6 as shown the integration of this signal. Moreover, the intensity of the signal decreases, when heavy water is added to a system. Location of the proton signals of the quinazoline and phenyl ring did not change significantly in the spectrum of ester and esterodiol (compare Figures 3 and 4).

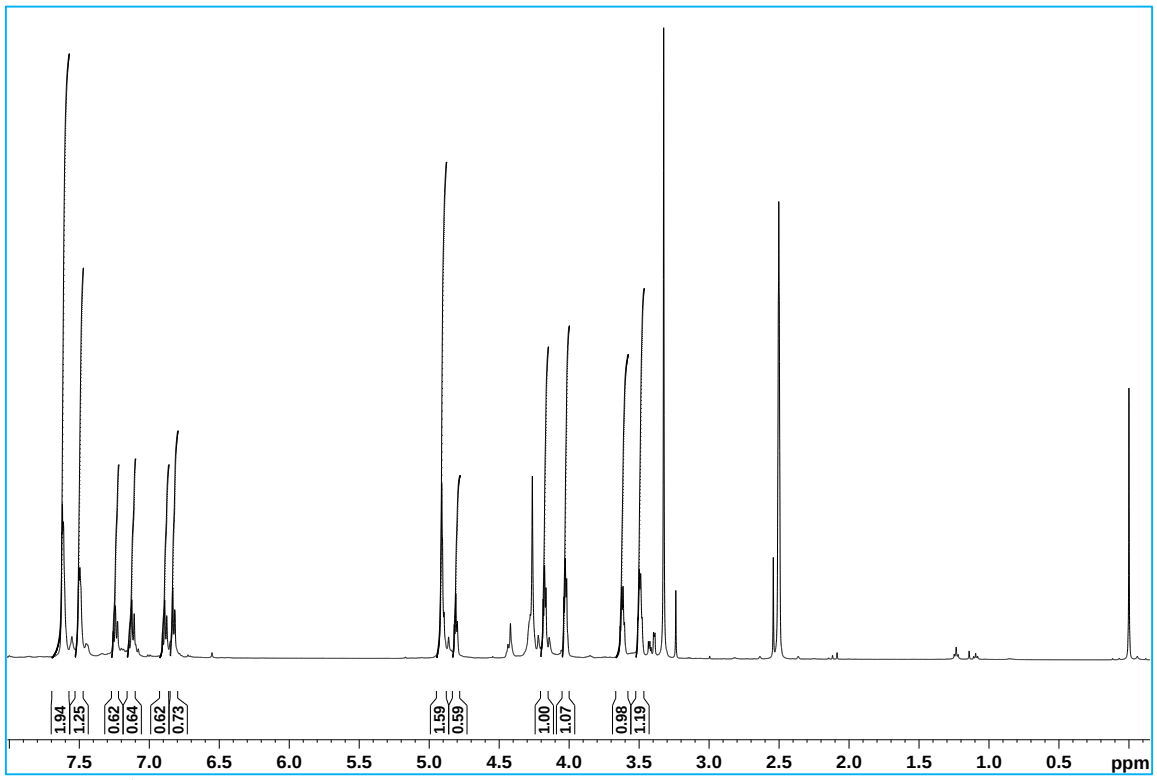

Figure 4 – ^{1}H-NMR spectrum of 2,6-bis[(2-hydroxyethoxy)carbonylmethyl]-1-phenylimidazo[1,5-c]quinazoline-3,5-dione

^{13}C-NMR spectrum of esterodiol also allows to confirm its structure (Fig. 5). There is observed no signals between 10 and 20 ppm, characteristic of the carbon atoms of methyl groups. All signals were identified on the spectrum (Fig. 5).

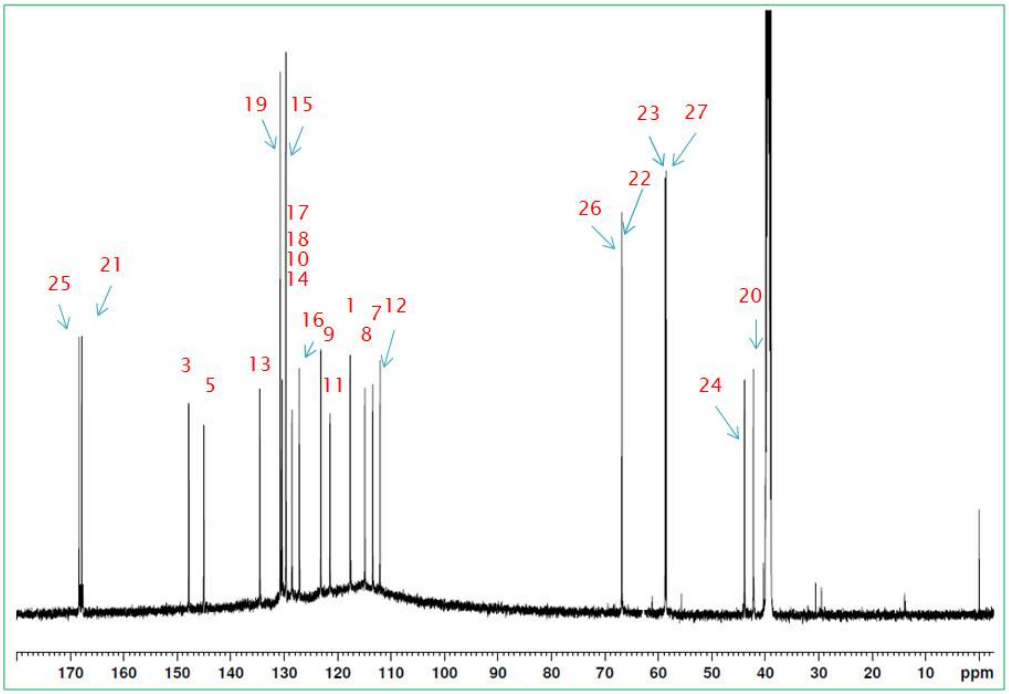

Figure 5 – ^{13}C-NMR spectrum of 2,6-bis[(2-hydroxyethoxy)carbonylmethyl]-1-phenylimidazo[1,5-c]quinazoline-3,5-dione

The infrared spectrum of esterodiol (Fig. 6) shows a characteristic band for vibration valence bond O-H of alcohol in the range of 3200-3700 cm^{-1}. Moreover, we can observed a valence vibrations band of the C-OH characteristic of primary alcohols at 1020 cm^{-1}. The valence vibration band of an ester carbonyl group occurs at 1747 cm^{-1}. The bands of the symmetrical and asymmetrical valence vibration C-O ester bond are observed at 1201 and 1072 cm^{-1}. The location of these bands does not change compared to the IR spectrum of the starting ester.

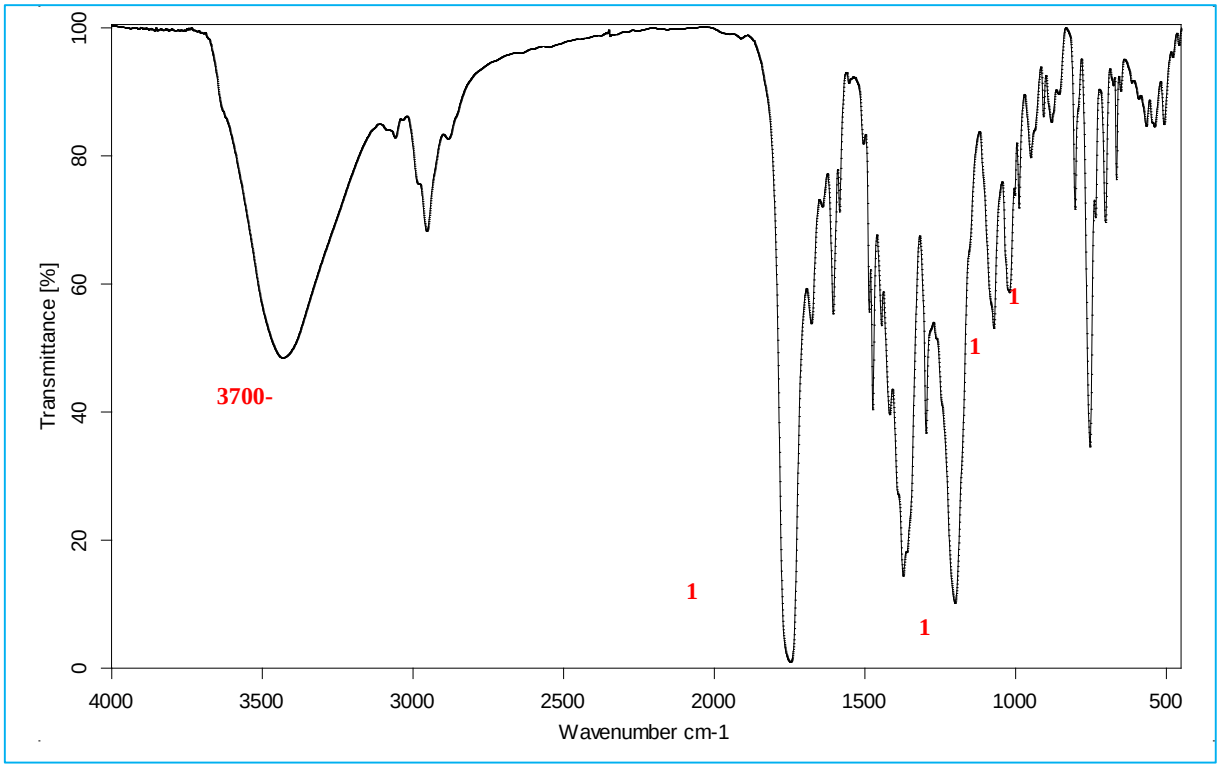

Figure 6 - IR Spectrum of 2,6-bis[(2-hydroxyethoxy)carbonylmethyl]-1-phenylimida-zo[1,5-c]quinazoline-3,5-dione

EXPERIMENTAL

1. Materials

2,6-bis(ethoxycarbonylmethyl)-1-phenylimidazo[1,5-c]quinazoline-3,5-dione was obtained from 1-phenyl-2H,6H-imidazo[1,5-c]quinazoline-3,5-dione [6] according to procedure [7].

Ethylene glycol, pure for analysis, POCH Poland.

Zinc acetate, pure for analysis, POCH Poland.

Acetone, pure for analysis, POCH Poland.

2. Synthesis of 2,6-bis((2-hydroxyethoxy)carbonylmethyl)-1-phenylimidazo[1,5-c]quinazoline-3,5-dione

2.225 g (5 mmol) of 2,6-bis(ethoxycarbonylmethyl)-1-phenylimidazo-[1,5-c]quinazoline-3,5-dione, 0.70 g (11 mmol) ethylene glycol, 0.004 g (0.02 mmol) zinc acetate, were placed into a three-necked flasks equipped with Dean Stark trap, reflux condenser, thermometer and mechanical stirrer. The reaction mixture was stirred and heated up to a temperature of 190 - 195°C in the presence of nitrogen atmosphere. Methanol, which released from the reaction mixture upon the transesterification process, was condensed and collected in the trap. Then the temperature was raised to 197 - 198°C and the excess ethylene glycol was distilled off. Next, a reaction flask was cooled in an inert atmosphere. The crude, solidified product was purified by crystallization from acetone.

The purity of substances were monitored by TLC (elution systems chloroform - ethanol, 9:1) on Alugram SIL G/UV254 foils (Macherey-Nagel).

3. Analytical methods

Melting points were measured in capillary apparatus.

Infrared spectrum (4000 − 400 cm^{-1}), obtained from KBr disks, were recorded on a Bruker ALPHA FT-IR instrument.

NMR spectra were recorded using Bruker 500 MHz spectrometer in DMSO-d_6. ^{1}H and ^{13}C chemical shifts are given on the δ scale (ppm) and are referenced to internal TMS.

Elemental analyses were carried out on an Elementar Vario ELIII instrument.

CONCLUSIONS

The transesterification reaction of 2,6-bis(methoxycarbonylmethyl)-1-phenyl-imidazo[1,5-c]quinazoline-3,5-dione with ethylene glycol afforded to obtain a new, previously unknown esterodiol - 2,6-bis[(2-hydroxyethoxy)carbonylmethyl]-1-phenylmidazo[1,5-c]quinazoline-3,5-dione. The structure of the new compound was confirmed by spectral methods. New esterodiol has a significantly higher solubility as compared to 1-phenyl-2H,6H-imidazo[1,5-c]quinazoline-3,5-dione, which gives the possibility of using its expected biological properties.

References

1 Zhang Y., Chen Z., Lou Y., Yo Y. 2,3-Disubstituted 8-arylamino-3H-imidazo[4,5-g]quinazolines: A novel class of antitumor agents. European Journal of Medicinal Chemistry. 2009, No. 44. P. 448-452.

2 Tortorella G., Piccinb A., Tieghi A. Marcheselli L., Steurer M., Gastl G., Codeluppi K., Famac A., Santorof U., Birtolog C., Gugliotta G., Cortelazzoi S., Gugliotta L. Anagrelide treatment and cardiovascular monitoring in essenatial thrombocythemia. A prospective observational study. Leukemia Research. 2015, No. 39. P. 592-598.

3 Stadlbauer W., Laschober R., Lutschounig H., Schindler G., Kappe T. Halogenation reactions in position 3 of quinoline-2,4-dione systems by electrophilic substitution and halogen exchange. Monatshefte fűr Chemie. 1992. No. 123. P. 617–636.

4 Mrkvicka V., Lycka A., Rudolf O., Klásek A. Reaction of 3-aminoquinoline-2,4-diones with isothiocyanic acid—an easy pathway to thioxo derivatives of imidazo[1,5-*c*]quinazolin-5-ones and imidazo[4,5-*c*]quinolin-4-ones. *Tetrahedron*. 2010. No 67. P. 8441-8445.

5 Mrkvicka V., Rudolf O., Lycka A., Klasek A. Reaction of 1-substituted 3-aminoquinolinediones with isocyanic and isothiocyanic acid. *Tetrahedron*. 2011. No 67. P. 2407-2413.

6 Klasek A., Koristek K., Lycka A., Holcapek M. Unprecedented reactivity of 3-amino-1H,3H-quinoline-2,4-diones with urea: an efficient synthesis of 2,6-dihydro-imidazo[1,5-c]quinazoline-3,5-diones. Tetrahedron. 2003. No 59. P. 1283-1288.

7 Szyszkowska A., Zarzyka I., A Klasek, Synthesis and characterization of ester with imidazoquinazoline ring, „львівскі хімічні читання – 2015”, 24-27 May 2015.

SPECTRAL CHARACTERIZATION OF 2,6-BIS(2-HYDROXYETHYL)IMIDAZO[1,5-*C*]QUINAZOLINE-3,5-DIONE

Szyszkowska A.

Rzeszow University od Technology,
Rzeszów, Poland

Zarzyka I.

Rzeszow University od Technology,
Rzeszów, Poland

ABSTRACT

The article presents the results of reactions 1-phenyl-2H,6H-imidazo[1,5-c]quinazoline-3,5-dione with 2 molar excess ethylene oxide, which gives 1-phenyl-2,6-bis(2-hydroxyethyl)imidazo[1,5-*c*]quinazoline-3,5-dione. The product was isolated at high yield from the reaction mixtures and identified on the basis of IR, ^{1}H-and ^{13}C-NMR spectroscopy. This compound can have biological activity or may be used for the synthesis of polymer.

KEYWORDS

imidazoquinazoline, diol, oxirane, hydroxyalkylation

INTRODUCTION

Recently, we may a growing interest in compounds containing: quinoline, quinazoline, imidazoquinoline, or imidazoquinazoline groups. Figure 1 shows mentioned structure. There are polyheterocyclic compounds containing nitrogen atoms in their rings. Quinolines and quinazolines are the precursors of new compounds such as imidazole derivatives thereof. Research indicates that both compounds containing imidazoquinoline and imidazoquinazoline group have interesting properties [1-3].