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RESEARCH ARTICLE

Preparation of 2-R 5-oxo5-*H*6-*N,N*-diethylcarboxamide 7-phenyl-[1,3,4]thiadiazolo-[3,2-a]pyrimidine and Study of Biological Properties

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Abstract: Preparation of 2-*R* 5-oxo 5-H 6 -*N,N*-diethylcarboxamide 7-phenyl 1,3,4-thiadiazolo-[3,2-a] pyrimidine through reaction of 2-R 5-Oxo 5-*H* 6- ethyl carboxilate 7-phenyl -1, 3,4 - thiadiazolo-[3,2-a] pyrimidine with *N,N*-diethylamin have been discussed in the paper. These compounds have many medicinal properties and are used in allergy medication and in anti-microbial studies. The structures of the compounds were elucidated using NMR, ^{13}C, IR- spectroscopy.

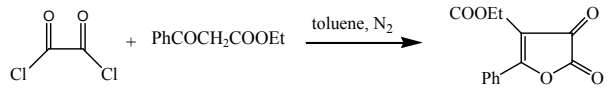
Keywords: 2-R 5-oxo 5-*H* 6-*N*, *N*-diethylcarboxamide 7-phenyl1,3,4-thiadiazolo-[3,2-a]pyrimidine, *N,N*-Diethylcarboxamide, NMR, Spectroscopy

Introduction

Derivatives of 1,3,4-thiadiazolo 3,2-alpyrimidine are potential biologically active substances[1-4]. Thiadiazoles and their condensed analogs are still insufficiently studied. In continuation of our search for substance possessing in creased ability to permeate through biological membranes of various infectious species[5,6] and in particular, for the new antibacterial drugs in these homologous series of compounds. We have prepared derivatives of 5-oxo-5*H*-1,3,4-thiadiazolo[3,2- a] pyrimidine.

The thiadiazolo pyrimidine nucleus and its substituted products, as well as a number of other substances belonging to the pseudo purine class were reported to have interesting biological propertie[7-14]. With the aim of extending our research on 1,3,4- thiadiazolo derivates of pharmacological interest. Various methods for obtaining this class of compounds have been reported[15-19]. The introduction of a substituent at position 6 of the1,3,4-thiadiazolo-[3,2-a] pyrimidine system efficiently enhances the physiological activity of the molecule[20,21]. This replacement occurs in the reactions of 1,3,4 -thiadiazolo [3,2-a] pyrimidine derivatives with elctrophiles[22,23].

We have prepared 2-R 5-oxo 5-H 6 -*N*,*N*-diethylcarboxamide7-phenyl 1,3,4-thiadiazolo-[3,2-a] pyrimidine in several stage. In the first step, we have synthesized ethyl-4,5-dioxo 2-phenyl 4,5-dihydrofuran 3-carboxylate (**3**) from oxalic acid dichloride compound (**1**) and benzoyl ethyl acetate (**2**) (Figure 1).



1 2 3

Figure 1. Synthesis of ethyl 4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate

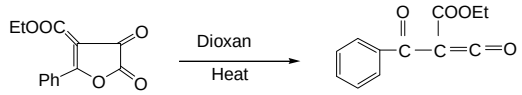


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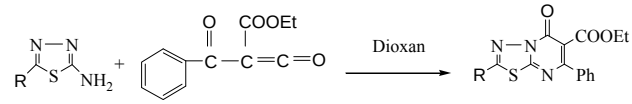
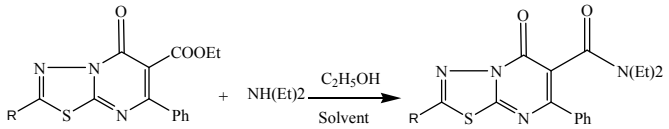
Figure 2. Synthesis of ethyl 2-formyl-3-oxo- 3- phenylpropanoate from of ethyl 4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate



5 6

R:(H ,CH_3, Ph- ,$PhCH_2$- ,Br)

Figure 3. Synthesis of derivatives of 2-R5-oxo 5-H 6- ethyl carboxylate7-phenyl-1,3,4-thiadiazolo [3,2- a]pyrimidine



7 8

R:(H ,CH_3, Ph- ,$PhCH_2$- ,Br)

Figure 4. Synthesis of 2- R 5-oxo 5-H 6-*N*,*N*-diethylcarboxamide7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine

In second stage, we have synthesized ethyl 2-formyl-3-oxo-3- phenylpropanoate (**4**) from of ethyl 4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate (Figure 2). In another stage we synthesized 2-R5-oxo5-H6-Ethylcarboxilate7-phenyl [1,3,4]thiadiazolo[3,2,-a]pyrimidine (**6**) with use of 2- R 5-amino 1,3,4-thiadiazole (**5**) and ethyl 2-formyl 3-oxo 3-phenyl propanoate (Figure 3). And finally2-R5-oxo5-H6-Ethylcarboxilate7-phenyl [1,3,4] thiadiazolo[3,2,-a]pyrimidine reacted with N,N-diethylamin (**7**) until produced 2-R 5-oxo 5-H 6-*N*,*N*-diethylcarboxamide7-phenyl 1,3,4-thiadiazolo-[3,2-a] pyrimidine (**8**) (Figure 4).

Experimental

A mixture of 2-R 5-oxo 5-*H* 6-ethylcarboxylate 7-phenyl 1,3,4- thiadiazolo [3,2-a] pyrimidine (1 mmol), *N*,*N*-diethylamin(1 mmol) was stirred magnetically at 78 ^{o}C and the progress of the reaction was monitored by thin-layer chromatography (TLC). The reaction mixture was filtered. In all the cases, the product obtained after the usual work up gave satisfactory spectral data.

For example,2-CH_3 5-oxo 5-H 6-ethylcarboxylate 7-phenyl 1,3,4- thiadiazolo [3,2-a] pyrimidine (1 mmol-0.314 g),*N*,*N*-diethylamin(1 mmol- 0.073 g) reacted together in ethanol at 78 ^oC. And the product was obtained in 87% yield.

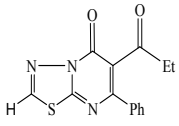
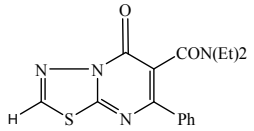
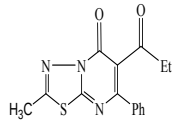
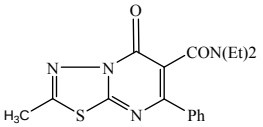
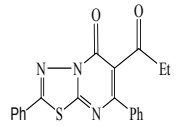
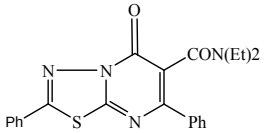
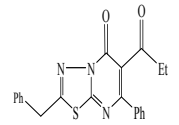
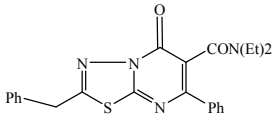
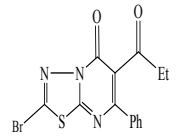
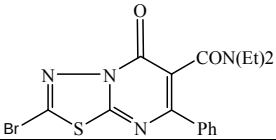
2-CH_3 5-oxo 5-H 6-N,N-diethyl carboxamide 7-phenyl -1,3,4-thiadiazolo [3,2-a] pyrimidine: ^1H NMR (400 MHz, $CDCl_3$, δ ppm): 0.9(s,3H,CH_3); 1.2(t,3H,CH_3); 3(q,2H,CH_2); 7.30-7.4630 (5H, Ph); - ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm):12.8(CH_3), 12.8(CH_3), 24.2(CH_3), 41(CH_3),41(CH_2), 118 (C), 126,4 (CH), 126,4 (CH), 128(CH), 128.7(CH), 128.7(CH), 136.9(C), 154.7(C), 159.8(C), 162.1(C), 163 (C), 168(C).

Results and Discussion

We tried to synthesis 2- R 5-oxo 5-H 6-*N*,*N*-diethylcarboxamide7-phenyl -1,3,4-thiadiazolo [3,2-a] pyrimidine with 2-R 5-oxo 5-H 6-ethylcarboxylate 7-phenyl 1 ,3,4-thiadiazolo [3,2-a] pyrimidine and *N*,*N*-diethylamin in various solvent. But alcohols were the best solvent to this reaction. The alcohols such as methanol and ethanol have more use.

To show the generality and applicability of this procedure, we treated a wide variety of 2- R 5-oxo 5-H 6-ethylcarboxylate 7-phenyl 1,3,4- thiadiazolo [3,2-a] pyrimidine and *N*,*N*-diethylamin in the presence of ethanol at 78 ^oC and obtained the desirable products in good to excellent yields (Table 1).

Table 1. Synthesis of 2- R 5-oxo 5-H 6-*N*,*N*-diethylcarboxamide7-phenyl -1,3,4-thiadiazolo [3,2-a] pyrimidine from 2- R 5-oxo 5-H 6-ethylcarboxylate 7-phenyl 1,3,4- thiadiazolo [3,2-a] pyrimidine and *N*,*N*-diethylamin[a]

Entry	Thiadiazol	*N*,*N*-diethylamin	Product	Time, h	Yield[b], %
1		NH(Et)2		8	87
2		NH(Et)2		7	87
3		NH(Et)2		7	84
4		NH(Et)2		6	90
5		NH(Et)2		8	86

[a]Reactions were carried out with 2- R 5-oxo 5-H 6-ethylcarboxylate 7-phenyl 1 ,3,4- thiadiazolo [3,2-a] pyrimidine and N,N-diethylamin, [b]Yields refer to isolated pure products

Conclusion

Compound 2-R 5-oxo 5-H 6-*N*,*N*-diethylcarboxamide7-phenyl -1,3,4-thiadiazolo [3,2-a] pyrimidine were prepared in excellent yields from 2- R 5-oxo 5-H 6-ethylcarboxylate 7-phenyl 1,3,4-thiadiazolo [3,2-a] pyrimidine and *N*,*N*-diethylamin that have a broad spectrum of antimicrobial activity. Therefore, these compounds can be useful in the search for new anti microbial drugs.

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