Synthesis of 2-R 5-oxo5-H6- N-ethylcarboxamide7-phenyl-[1,3,4]thiadiazolo-[3,2-a]pyrimidine and 2-R 5-oxo5-H6- N-methylcarboxamide 7-phenyl-[1,3,4]thiadiazolo-[3,2-a]pyrimidine and Biological properties

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ABSTRACT: In this paper explain preparation of 2-R 5-oxo5-H6-N-ethylcarboxamide 7-phenyl,3,4-thiadiazolo-[3,2-a] pyrimidine and 2-R 5-oxo 5-H 6-N-methyl carboxamide 7-phenyl 1,3,4-thiadiazolo-[3,2-a] pyrimidine through reaction of 2-R 5-Oxo5-H 6- ethylcarboxilate 7 - phenyl -1, 3, 4 -thiadiazolo-[3,2-a] pyrimidine with N-ethylamine and N-methylamine. Interest in the synthesis of pyrimidine derivatives is due to their biological activities. These compounds have many medicinal properties and are used in allergy.

Keywords: Pyrimidine, N-ethylcarboxamide-N-methylcarboxamide, Medicinal properties, Synthesis, Spectroscopy.

INTRODUCTION

Condensed derivatives of 1,3,4-thiadiazolo-[3,2-a]pyrimidine were reported to possess a broad spectrum of biological activity [1–4], including antibacterial, antitumor, fungicidal, and herbicidal properties. However, thiadiazoles and their condensed analogs are still insufficiently studied. In continuation of the search for substances possessing increased ability to permeate through biological membranes of various infectious species [5–7] and, in particular, for the new antibacterial drugs in these homologous series of compounds, 1,3,4-thiadiazolo [3,2-a] pyrimidine system efficiently enhances the physiological activity of the molecule[ 8-10].

This replacement occurs in the reactions of 1,3,4-thiadiazolo [3,2-a] pyrimidine derivatives with electrophiles [11,12], at position 6 of the Literature data on fused heterocycles with a thiadiazolo-[3,2-a] pyrimidine system unrelated with antherring are scarce. These include 1,3,4-thiadiazolo-[2,3 -b] quinozalines,[13-15] pyrazol[3 ,4-e]1,3,4-thiadiazolo-[3,2-a] pyrimidines, [16] and 1,3,4-thiadiazolo-[3,2-a] pyrido [3,2-e] pyrimidines [17].

Derivatives of 1,3,4-thiadiazolo-[3,2-a] pyrimidine are potential biologically active substances [18-26]. The introduction of ketene dithioacetal fragments into the molecules makes it possible to synthesize heterocyclic systems with various functional groups [27, 28].

We Synthesis 2-R 5-oxo 5-H 6-N-ethylcarboxamide, N-methylcarboxamide7-phenyl 1,3,4-thiadiazolo-[3,2-a] Pyrimidine in multi-stage (Scheme 1).
RESULTS AND DISCUSSION

we synthesized 2-R5-oxo5-H6-N-ethylcarboxamide,N-methylcarboxamide7-phenyl 1,3,4-thiadiazolo[3,2-a] pyrimidine from 2-R5-oxo5-H 6-ethylcarboxylate 7-phenyl1,3,4-thiadiazolo[3,2-a] pyrimidine and N-ethylamine and N-methylamine in various solvent. But alcohols are the best solvents to this reaction. The alcohols such as methanol and ethanol have more use. This compounds (2- R5-oxo5-H6-N-ethylcarboxamide, N-methylcarboxamide7-phenyl 1,3,4-thiadiazolo[3,2-a] pyrimidine) can be useful in the search for new antimicrobial drugs. The antimicrobial activity of thiadiazolo pyrimidine (1-16) was studied with respect to a series of test microbes. The antibacterial activity was evaluated by broth micro dilution susceptibility tests as recommended by clinical laboratory standard institute (CLSI) for determination of the minimum concentration of samples required for inhibition of visible growth of bacteria. The data obtained show that compounds 2-R5-oxo5-H6-N-ethylcarboxamide, N-methylcarboxamide7-phenyl 1,3,4-thiadiazolo[3,2-a] pyrimidine, have antimicrobial Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli and etc.
Table 1: Synthesis of 2-R 5-oxo 6-N-ethylcarboxamide 7-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-ethylamin.

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<th>Product</th>
<th>Time(h)</th>
<th>Yield(%)</th>
<th>Melting point</th>
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* 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-ethylamin

*Yields refer to isolated pure products
Table 2. Synthesis of 2-R 5-oxo 5-H 6-N-methylcarboxamide 7-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-methylcarboxamide a.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Thiadiazol pyrimidine</th>
<th>N-methylamin</th>
<th>Product</th>
<th>Time(h)</th>
<th>Yield(%)</th>
<th>Melting point</th>
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<td><img src="image16" alt="Product" /></td>
<td>7</td>
<td>90</td>
<td>173-175</td>
</tr>
</tbody>
</table>

*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-methylamin.

*Yields refer to isolated pure products*
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-ethylaminandN-methylaminin the presence of alcohol ethanol at 78°C and obtained the desirable products in good to excellent yields (Table 1,2).

Scheme 2. Mechanism of reaction for Synthesis of 2-Benzyl 5-Oxo 5-H 6-R-amide derivatives 7-phenyl 1,3,4-thiadiazolo-[3,2-a]- pyrimidine.
EXPERIMENTAL

For the synthesis 2-R 5-oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine. For example, for the synthesis 2-Pb 5-oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine, first: oxalic acid dichloride (1.0.127 g) and ethyl benzylacetate (0.86mmol,0.165g) reacted together in toluene at 110°C until is produced ethyl-4.5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate(0.23g,92%) and in another stage ethyl-4.5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate (1mmol,0.25g) in boiling dioxan converted to ethyl-2-formyl-3-oxo-3-phenyl propanoate (that is isopen cycle). At more mixture of 2-Pb5-amino-1,3,4-thiadiazole (1mmol, 0.177g), ethyl-2-formyl-3-oxo-3-phenylpropanoate (1mmol,0.218g) was stirred magnetically in toluene at 110°C for 10-14 hours (12h) and the progress of the reaction was monitored by thin-layer chromatography (TLC). The reaction mixture was filtered. In all the cases, the product 2-Pb5-oxo 5-H 6-ethylcarboxylate 7-phenyl 1,3,4-thiadiazolo-136.9(C), 154.7(C), 159 .8(C), 162.1(C), 163 (C), 168(C). A mixture of 2-Pb 5-oxo 5-H 6-ethylcarboxylate 7-phenyl 1,3,4-thiadiazolo [3,2-a] pyrimidine (1mmol,0.391g) and N-ethylamin (1mmol,0.045g) was stirred magnetically at 78°C and the progress of the reaction was monitored by thin-layer chromatography (TLC). The reaction mixture was filtered. The product obtained after the usual work up gave satisfactory spectral data. And the production obtained in (0.357g, 95% yield).

A. Spectral data

1)-2-H 5-oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: 1H NMR (400 MHz, CDCl3, δ ppm): 1.2(t,3H,CH3 );3.1(q,2H,CH4 );1.5-7.40 (5H, Ph);7.55(s, H, CH);8.21(H,1H,NH) ; -13C NMR (100 MHz, CDCl3, δ ppm):15.1(CH3), 34.2(CH2), 118 (C), 126,4 (CH, 126,4 (CH) ,128(CH), 128.7(CH), 128.3(CH), 136.9(C), 140.4(CH)). 159 .8(C),162.1(C), 163 (C),168(C).

2)-2-CH3 5-oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: 1H NMR (400 MHz, CDCl3, δ ppm): 0.9(s,3H,CH3 ); 1.2(t,3H,CH3 );3(q,2H,CH4 );7.30-7.46 (5H, Ph);8.21(H,1H,NH) ; -13C NMR (100 MHz, CDCl3, δ ppm):15(CH3), 24.2(CH3), 34(CH2),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).

3)-2-Ph 5-oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: 1H NMR (400 MHz, CDCl3, δ ppm): 1.3(t,3H,CH3 );3.2(q,2H,CH2); 7.30-7.50 (10H, 2Ph);8.31(1H,NH) ; -13C NMR (100 MHz, CDCl3, δ ppm):15.1(CH3), 34.2(CH2), 118 (C), 126,4 (CH), 126,4 (CH) ,128(CH), 128.7(CH), 128.7(CH), 128.9(CH), 128.9(CH), 129.2(CH),129.2(CH), 130.7(C), 136.9(C), 143.7(C), 159 .8(C), 162.1(C), 163 (C),168(C).

4)-2-PhCH2 5-oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: 1H NMR (400 MHz, CDCl3, δ ppm): 1.2(t,3H,CH3 ); 2.6(s,2H,CH2); 3(q,2H,CH3 );7.07-7.50 (10H,2Ph);8.11(1H,NH) ; -13C NMR (100 MHz, CDCl3, δ ppm):15(CH3), 34.2(CH2), 38.2(CH2),118 (C),125.8 (CH ) ,126,4 (CH) ,126.4 (CH) ,128(CH) ,128.7(CH) ,128.7(CH) ,128,7(CH), 129.1(CH),129.1(CH), 136.9(C),137.5(C),145.6(C), 159 .8(C), 162.1(C), 163 (C),168(C).

5)-2-Br 5-oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: 1H NMR (400 MHz, CDCl3, δ ppm): 1.2(t,3H,CH3 );3(q,2H,CH2) ; 7.14-7.30 (5H, Ph);8.21(1H,NH) ; -13C NMR (100 MHz, CDCl3, δ ppm):15(CH3), 34(CH2),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).

6)-2-CH2O 5-Oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: 1H NMR (400 MHz, CDCl3, δ ppm): 1.2(t,3H,CH3 );3(q,2H,CH2) ;3(q,2H,CH2) ;7.14-7.35 (5H, Ph);8.21(1H,NH); -13C NMR (100 MHz, CDCl3, δ ppm):15(CH3), 34(CH2), 47.3(CH2),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).

7)-2-ETO 5-Oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: 1H NMR (400 MHz, CDCl3, δ ppm): 1.01(t,3H,CH3); 1.2(t,3H,CH3 );3(q,2H,CH2) ;3.4(q,2H,CH2) ;7.15-7.30 (5H, Ph);8.21(1H,NH); -13C NMR (100 MHz, CDCl3, δ ppm):14.6(CH3), 15.1(CH3), 34.2(CH2), 57.3(CH2),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).

8)-2-C6H5F 5-Oxo 5-H 6-N-ethylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: 1H NMR (400 MHz, CDCl3, δ ppm): 1.2(t,3H,CH3);3(q,2H,CH2) ;7.15-7.65 (10H,2Ph);8.11(1H,NH); -13C NMR (100 MHz, CDCl3, δ ppm):15.1(CH3), 34.2(CH2),115.6 (CH),115.6 (CH), 118 (C),126,4 (CH),126,4 (CH) ,128(CH) ,128.7(CH), 128.7(CH), 130.8(CH), 130.8(CH),136.9(C),143.8(C),159 .8(C), 162.1(C), 163 (C),165.2(C),168(C).
The preliminary results showed that oxo 5-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine. H NMR (400 MHz, CDCl3, δ ppm): 2.7(s,3H,CH3); 7.15-7.40 (5H, Ph); 7.55 (s, 2H, CH); 8.2(1H,NH); - 13C NMR (100 MHz, CDCl3, δ ppm): 26.1(CH3), 118 (C), 126.4 (CH), 126.4 (CH), 128.7 (CH), 128.7 (CH), 136.9 (C), 140.4 (CH), 159.8(C), 162.1(C), 163(C), 168(C).

10)-2-CH3 5-oxo 5-H 6-N-Methylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: H NMR (400 MHz, CDCl3, δ ppm): 0.9(s,3H,CH3); 2.7(s,3H,CH3); 7.15-7.6 (10H, 2Ph); 8.2(1H,NH); - 13C NMR (100 MHz, CDCl3, δ ppm): 26.3(CH3), 118 (C), 126.4 (CH), 126.4 (CH), 128.7 (CH), 128.7 (CH), 128.9 (CH), 129.2 (CH), 129.2 (CH), 130.7(C), 131.1(C), 136.9 (C), 143.7(C), 159.8(C), 162.1(C), 163(C), 168(C).

11)-2-Ph 5-oxo 5-H 6-N-Methylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: H NMR (400 MHz, CDCl3, δ ppm): 2.7(s,3H,CH3); 7.15-7.6 (10H, 2Ph); 8.2(1H,NH); - 13C NMR (100 MHz, CDCl3, δ ppm): 26.3(CH3), 118 (C), 126.4 (CH), 126.4 (CH), 128.7 (CH), 128.7 (CH), 128.9 (CH), 129.2 (CH), 129.2 (CH), 130.7(C), 131.1(C), 136.9 (C), 143.7(C), 159.8(C), 162.1(C), 163(C), 168(C).

12)-2-PhCH3 5-oxo 5-H 6-N-Methylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: H NMR (400 MHz, CDCl3, δ ppm): 2.7(s,3H,CH3); 7.14-7.65 (10H, 2Ph); 8.1(1H,NH); - 13C NMR (100 MHz, CDCl3, δ ppm): 26.3(CH3), 38.2(CH2), 118 (C), 125.8 (CH), 126.4 (CH), 126.4 (CH), 128.7 (CH), 128.7 (CH), 129.1 (CH), 129.1 (CH), 136.9(C), 137.5(C), 145.8(C), 159.8(C), 162.1(C), 163(C), 168(C).

13)-2-Br 5-oxo 5-H 6-N-Methylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: H NMR (400 MHz, CDCl3, δ ppm): 2.7(s,3H,CH3); 7.14-7.30 (5H, Ph); 8.1(1H,NH); - 13C NMR (100 MHz, CDCl3, δ ppm): 26.3(CH3), 118 (C), 126.4 (CH), 126.4 (CH), 128.7 (CH), 128.7 (CH), 136.9(C), 154.7(C), 159.8(C), 162.1(C), 163(C), 168(C).

14)-2-CH2O 5-Oxo 5-H 6-N-Methylcarboxamide 7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine: H NMR (400 MHz, CDCl3, δ ppm): 2.7(s,3H,CH3); 3.4(s,3H,CH3); 7.14-7.35 (5H, Ph); 8.2(1H,NH); - 13C NMR (100 MHz, CDCl3, δ ppm): 26.2(CH3), 47.7(CH3), 118 (C), 126.4 (CH), 126.4 (CH), 128(CH), 128.7 (CH), 136.9(C), 154.7(C), 159.8(C), 162.1(C), 163(C), 168(C).

CONCLUSIONS

In the present work, we design and discover a new class of 2-R 5-oxo 5-H 6-N-methylcarboxamide-7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine and 2-R 5-oxo 5-H 6-N-ethylcarboxamide-7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine. The preliminary results showed that most of this synthesis, various alcohols have been employed as a mild and highly efficient solvent system for the convenient preparation of 2-R 5-oxo 5-H 6-N-methylcarboxamide-7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine and 2-R 5-oxo 5-H 6-N-ethylcarboxamide-7-phenyl-1,3,4-thiadiazolo [3,2-a] pyrimidine and N-ethylaminand N-methylamin. The advantages include low cost, mild reaction conditions and with excellent yields. The antimicrobial activity of 2-R5-Oxo 5-H 6-Amide derivatives-7-phenyl 1,3,4- thiadiazolo-[3,2-a]-pyrimidine (1-16) was studied with respect to a series of test microbes.

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