



Synthesis and characterization of heterocyclic oxo-pyrrolidine based compound

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Abstract:

N-containing heterocyclic compounds play a unique role in various domains of human activity, among the N-containing heterocyclic compounds, oxopyrrolidin has attracted significant attention in recent years because incorporation of a number of pharmacologically active compounds. In this article, heterocyclic oxo-pyrrolidine has been synthesized from 3,5-diaminobenzoic acid in good yield and characterized by spectroscopy techniques.

Key words: Oxo-pyrrolidine, amide, lactam, amino acid.

Introduction:

Heterocyclic compounds are the most significant class of organic compounds that play a key role in drug discovery and biological function because heterocyclic compounds have an exclusive chemical properties that allows them to be broadly used in drug development.¹ Among the N-containing heterocyclic compounds, pyrrolidine is N-containing five membered lactam ring which is constructed in several pharmaceutical drug synthesis and active natural products. In recent times, substantial efforts were directed toward the growth of anticancer agents carrying the pyrrolidone core, targeting numerous malignancies such as colorectal (HCT116),² breast,³ hepatic (SMMC-7721) and cervical (HeLa) cancers.⁴ Pyrrolidinone heterocyclic exhibited a wide range of biological activities such as antifungal,⁵ antibacterial.⁶ Anticonvulsant,⁷ growth-stimulating, herbicide,⁸ antiarrhythmic,⁹ antihypertensive,¹⁰ neuroprotective attributes, especially in the

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context of Alzheimer's disease.¹¹ Azaspirene is a angiogenesis inhibitor which is detached from the fungus *Neosartorya* sp.¹² Apart from this, substituted 3-pyrroline-2-ones with a 2-pyrrolidinone subdivision are also of great interest in medicinal chemistry as plentiful derivatives have exhibited historic pharmacological and biological potency, as a antitumours,¹³ anti-microbial,¹⁴ anti-inflammatory,¹⁵ anti-cancer agents,¹⁶ anti-bacterial,¹⁷ and HIV-1 integrase inhibitors.¹⁸ A pyrrolidine based drugs are shown in **figure 1**.¹⁹ The estimated various synthetic methods of oxo-pyrrolidine has been reported.²⁰ We synthesised a oxo-pyrrolidine substituted compound and characterised by spectroscopic method.

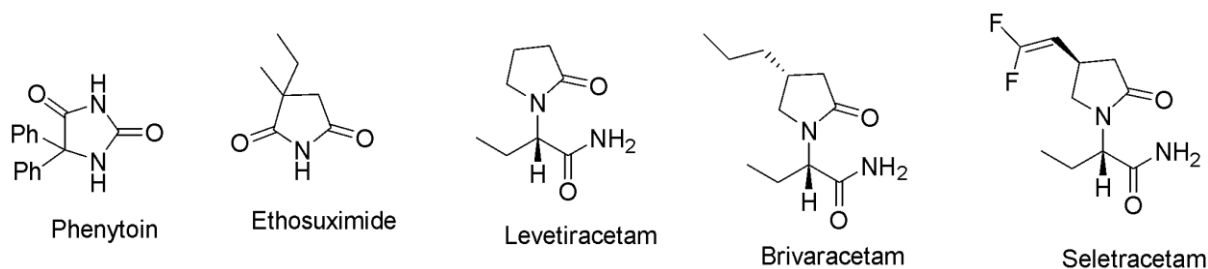


Figure 1. Heterocyclic oxo-pyrrolidine based drugs.

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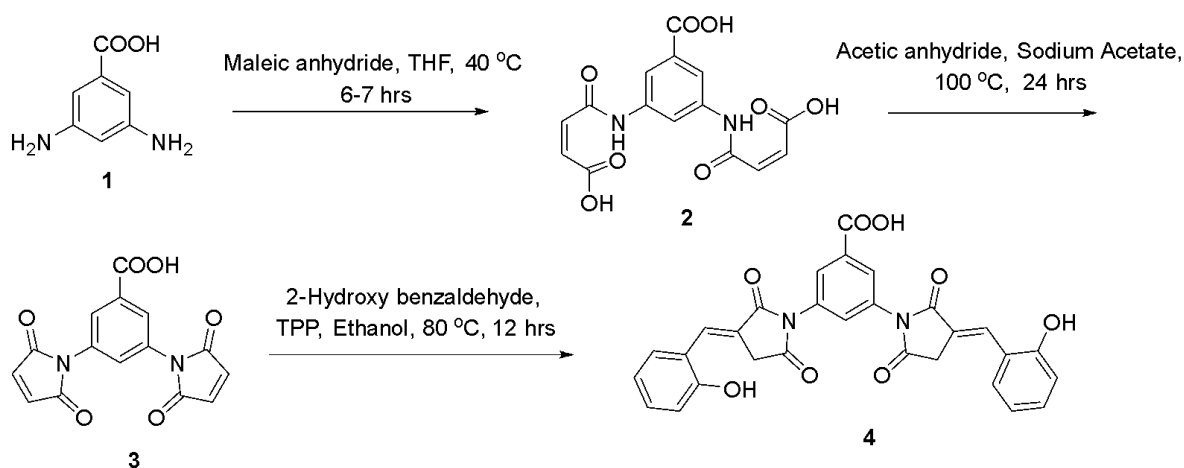
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Result and Discussion:

. The desired compound oxo-pyrrolidine substituted benzoic acid **4** was synthesised from 3,5-diaminobenzoic acid (**1**) in three steps (**Scheme 1**). Firstly, compound 3,5-diaminobenzoic acid (**1**) was dissolved in tetrahydrofuran solvent then added maleic anhydride and stirred the reaction mixture at 40 °C for 6-7 h. After completion of reaction mixture, solvent was removed by rotatory evaporator, then extracted the crude product **2** with chloroform and water. Organic layer came in chloroform solvent and again removed chloroform solvent by rotatory evaporator and purified the crude product **2** by column chromatography with methanol and chloroform solvent using silica gel in 95% yield. The characteristics proton of compound **2** in $^1\text{H-NMR}$ spectroscopy appeared at δ 6.27 and 6.38 (unsaturation $\text{CH}=\text{CH}$), 7.39 (aromatic proton), 8.26 (NH), 10.69 (OH) and $^{13}\text{C-NMR}$ appeared at δ 166 ($\text{C}=\text{O}$), 136 and 138 (unsaturation $\text{CH}=\text{CH}$), 118, 130 and 136 (aromatic carbon). The characteristics frequency in cm^{-1} in Infrared Spectroscopy appeared at 1670 (amide group, $\text{C}=\text{O}$), 1720 (carboxylic acid, $\text{C}=\text{O}$), 3120 (aromatic, C-H).

In the second step, compound **2** was treated with acetic anhydride and base sodium acetate at 100 °C for 24 h. After completion of reaction mixture, crude product **3** was extracted with chloroform and water. Organic layer came in chloroform solvent and removed the chloroform by rotatory evaporator and purified the crude product **3** by silica gel column chromatography using eluent solvent chloroform and methanol in 92% yield. The characteristics proton of compound **3** in $^1\text{H-NMR}$ spectroscopy appeared at δ 7.21 (oxopyrrolidine, $\text{CH}=\text{CH}$), 7.63 (aromatic proton), 7.96 (aromatic proton), 10.12 (carboxylic acid proton). In $^{13}\text{C-NMR}$ appeared at δ 169 ($\text{C}=\text{O}$, carboxylic), 161 (amide $\text{C}=\text{O}$), 135 ($\text{CH}=\text{CH}$, carbon). 115, 130, and 132 (aromatic carbon). The characteristics frequency in cm^{-1} in Infrared Spectroscopy appeared at 1676 (amide group, $\text{C}=\text{O}$), 1725 (carboxylic acid, $\text{C}=\text{O}$), 3123 (aromatic, C-H).



Scheme 1. Synthesis of substituted dioxopyrrolidin compound **4**.

The lastly desired compound **4** was achieved from the reaction between compound **3** and 2-Hydroxy benzaldehyde with TPP in ethanol solvent. Compound **3** was dissolved in ethanol then added 2-Hydroxy benzaldehyde and TPP and refluxed the reaction mixture for 12 h at 80 °C. After completion of reaction mixture, removed the solvent using rotatory evaporator and extracted the crude compound **4** by chloroform and water solvent. Organic layer came in chloroform solvent and again evaporate the chloroform by rotatory evaporator and purified the crude product **4** by using silica gel column chromatography using eluent solvent chloroform and methanol in 86% yield. The characteristics proton of compound **4** in ^1H -NMR spectroscopy appeared at δ 10.27 (OH), 7.75 ($\text{CH}=\text{C}$), 8.19, 6.90, 7.06, 7.49 (aromatic proton). In ^{13}C -NMR appeared at δ 171 (amide carbon), 169 (carboxylic carbon), 115, 118, 135 (aromatic carbon). The characteristics frequency in cm^{-1} in Infrared Spectroscopy appeared at 1708 (lactam, $\text{C}=\text{O}$), 1723 (carboxylic acid, $\text{C}=\text{O}$), 3127 (aromatic, C-H), 3380 (OH).

Conclusion:

In summary, we have synthesised a desired compound oxo-pyrrolidine substituted compound in three steps from 3,5-diaminobenzoic acid in good yield. The synthesised compound has been characterised by ^1H -NMR, ^{13}C -NMR and FT IR spectroscopy techniques. This compound may be useful for therapeutic applications.