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Synthesis of Novel sulfanamide 4-Thiazolidinone hybrides

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Abstract

A series of Novel sulfonamide 4-thiazolidinone hybrids were synthesized by reaction of various substited sufonyl chloride with 3-(4-nitrophenyl)-2-((2,2,3-trimethylcyclopent-3-en-1-yl)methyl)thiazolidin-4-one in the presence of DMF, MK-10 as acid catalyst. The compounds were characterized by spectral data such as NMR, and Mass spectroscopic.

Keywords: *4-thiazolidinone, sulfamethoxazole.*

1. Introduction

Sulfonamides are an important class of synthetic bacteriostatic antibiotics still used today for the treatment of bacterial infections and those caused by other microorganisms. They are also known as sulfa drugs and were the main source of therapy against bacterial infections before the introduction of penicillin in 1941.The presence of sulfur in the sulfonamide as well as thiazolidin-4-one moieties of the titled compounds was expected to increase the lipophilicity, consequently elevating drug concentration in the brain. a number of sulfonamides incorporating thiazolidin-4-ones have been synthesized reaction of various substited sufonyl chloride with 3-(4-nitrophenyl)-2-((2,2,3-trimethylcyclopent-3-en-1-yl)methyl)thiazolidin-4-one in the presence of DMF, MK-10 as acid catalyst and characterized by ^{1}H NMR, ^{13}C NMR, and mass spectroscopic anaylsis.

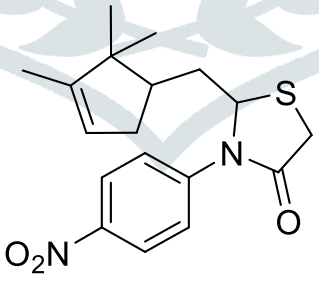

Figure 1: Structure of 4-thiazolidinone

2. Materials and Methodology

All chemical reagents and solvents were procured from Acros, Fisher Scientific and Sigma-Aldrich, etc., which were directly used as such without any purification. All the reactions were carried out under inert conditions. Isolated the products through crystallization, and precipitation techniques and purify the products through column chromatography. Calculate the percentage of yields based on pure products. Silica gel (100-200 mesh) is used as a solid phase for column chromatography. Precoated silica aluminum sheets were used for TLC. Identify the product on the TLC plate by using an Iodine or UV cabinet. The NMR spectrum was recorded on 400 MHz Bruker by using solvents CDCl3 or DMSO-d6, Mass spectrum on Apex, and IR spectrum on Bruker. Melting Points were determined for the compounds and are uncorrected.

Stage 1

Synthesis of 3-(4-nitrophenyl)-2-((2,2,3-trimethylcyclopent-3-en-1-yl)methyl)thiazolidin-4-one:

Campholenic aldehyde(10mmol), nitroaniline(10mmole) Compound 3a (0.0129 mol) and thioglycolic acid (20mmol) in DMF (5 ml) in the presence of MK-10 as acid catalyst were first stirred on a magnetic stirrer for 2.0 h at room temperature followed by refluxing on a steam bath at 70–90 °C for 6.0 h. The completion of the reaction was monitored using silica gel-G coated TLC plates. The product was filtered, extracted with ethylacetate and washed with hexane. The purified product was dried under vacuum and recrystallized from ethanol at room temperature to furnish compound.

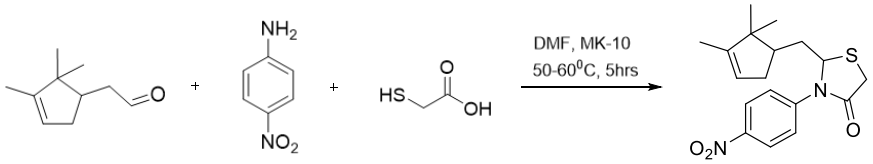

Fig 2: synthesis of 4-thiazolidinone

Stage 2

Synthesis of 3- (4- aminophenyl)- 2- ((2,2,3- trimethylcyclopent- 3- en- 1- yl)methyl)thiazolidin-4-one:

2gms tin in ethanol and 3M HCl was stirred and heated to 70°C to become clear solution. To this hot solution addition of 3- (4-nitrophenyl)-2- ((2,2,3-trimethylcyclopent-3-en-1-yl)methyl) thiazolidin-4-one and the mixture was heated for 1.5 hrs. No starting matrial remained by tlc analysis.

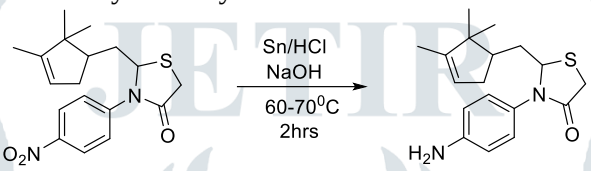

Fig 2: synthesis of amine 4-thiazolidinone

Stage 3

Synthesis of N- (4- (4-oxo-2- ((2,2,3- trimethylcyclopent-3- en-1-yl) methyl) thiazolidin-3-yl)phenyl)benzenesulfonamide derivatives:

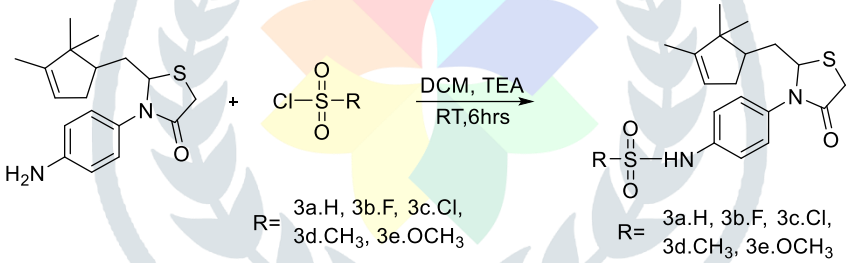

Fig 3: synthesis of sulphonoamide 4-thiazolidinone

3. Results and Discussion

3.1. Synthesis of 3- (4-nitrophenyl)-2- ((2,2,3- trimethylcyclopent-3- en-1-yl)methyl)thiazolidin-4-one:

viscous oil, yield 70%, **^{1}H NMR (400 MHz,) in DMSO-d$_6$:** δ 7.24 (2H, d, *J* = 3.3 Hz), 6.84 (2H, d, *J* = 8.1 Hz), 5.19 – 4.71 (1H, m), 4.42 – 4.06 (1H, m), 3.83 (2H, s), 1.70 (3H, s), 1.52 – 1.40 (2H, m), 1.24 – 1.16 (1H, m), 1.00 (6H, S).

^{13} C NMR DMSO-400HZ: δ 164.40, 146.85, 146.00, 138.22, 138.00, 120.36, 118.50, 57.75, 44.60, 35.51, 28.86, 20.68, 17.45.

Mass: 347.44(m/z)

3.2. Synthesis of 3- (4- aminophenyl)- 2- ((2,2,3- trimethylcyclopent- 3- en- 1- yl)methyl)thiazolidin-4-one:

Brown coloured , melting point 383.57^0 C, Yeild 85%, **^{1}H NMR (400 MHz,) in DMSO-d$_6$** : δ 6.47 (2H, d, *J* = 26.0 Hz), 6.00 (2H, d, *J* = 31.3 Hz), 5.32-5.25 (1H, m), 4.51 – 4.40 (1H, m), 3.87 (2H, s), 1.73 (5H, m), 1.67 (2H, m), 1.55-1.53 (1H, m), 0.79(6H, s).

^{13} C NMR DMSO-400HZ: δ 164.35, 146.76, 143.86, 138.21, 123.01, 120.27, 59.86, 45.82, 43.71, 32.65, 24.43, 17.40.

Mass: 317.33 (m/z).

3.3A. Synthesis of N- (4-(4-oxo-2- ((2,2,3-trimethylcyclopent-3-en-1-yl) methyl) thiazolidin-3-yl)phenyl)benzenesulfonamide:

Light yellow-green ppt, Melting point 447.01^{0}C**,** Yield 72.5%**, ^{1}H NMR (400 MHz,) in DMSO-d$_6$:** δ 9.93 (1H, s), 8.07 (2H, d, *J* = 7.5 Hz), 7.52 (2H, d, *J* = 7.7 Hz), 7.23 (2H, d, *J* = 7.6 Hz), 6.64 (2H, d, *J* = 6.8 Hz), 6.37 (2H, d, *J* = 1.2 Hz), 5.07-5.04 (1H, m), 3.84 (2H, s), 1.74 (5H, m), 1.68 – 1.61 (2H, m), 1.58 – 1.53 (1H, m), 1.05 (6H, s).

^{13} C NMR DMSO-400HZ: δ 164.35, 146.76, 143.86, 141.40, 138.21, 131.57, 130.84, 129.70, 128.55, 125.99,124.83, 123.01, 120.27, 59.86, 45.82, 43.71, 32.65, 24.43, 17.40.
Mass: 393.40 (m/z)

3.3B. Synthesis of 4- fluoro- N- (4-(4-oxo-2- ((2,2,3-trimethylcyclopent-3-en-1-yl)methyl) thiazolidin-3-yl)phenyl)benzenesulfonamide:
Pinkish -blue ppt, Melting point 452.25^{0}C, **^{1}H NMR (400 MHz,) in DMSO-d_6:** δ 10.17(s), 8.09 (2H, d, *J* = 8.2 Hz), 7.24 (2H, d, *J* = 1.0 Hz), 7.14 (2H, d, *J* = 1.5 Hz), 7.10 (2H, d, *J* = 1.5 Hz), 5.89 – 5.86 (1H, m), 4.28 – 4.25 (2H, m), 3.93 – 3.91 (2H, S), 1.88 – 1.85 (5H, m), 1.46 – 1.44 (2H, m), 1.42 – 1.41 (1H, m), 0.80 (6H, s).
^{13} C NMR DMSO-400HZ: δ 164.35, 146.76, 143.86, 141.40, 138.21, 131.57, 130.84, 129.70, 128.55, 125.99,124.83, 123.01, 120.27, 59.86, 45.82, 43.71, 32.65, 24.43, 17.40.
Mass: 475.15(m/z)

3.3C. Synthesis of 4- chloro- N- (4-(4-oxo-2- ((2,2,3- trimethylcyclopent-3-en-1-yl)methyl)thiazolidin-3-yl)phenyl)benzenesulfonamide:
Light pink-white ppt, Melting point 450.96^{0}C, **^{1}H NMR (400 MHz,) in DMSO-d_6:** δ 10.83 (1H, s), 8.09 (2H, d, J = 8.2 Hz), 7.24 (2H, d, J = 1.0 Hz), 7.14 (2H, d, J = 1.5 Hz), 7.10 (2H, d, J = 1.5 Hz), 5.90 – 5.86 (1H, m), 4.29 – 4.26 (1H, m), 3.92 (2H, S), 1.89 – 1.85 (5H, m), 1.46 – 1.44 (2H, m), 1.42 – 1.41 (1H, m), 0.80 (6H, s).
^{13} C NMR DMSO-400HZ: δ 164.35, 146.76, 143.86, 141.40, 138.21, 131.57, 130.84, 129.70, 128.55, 125.99,124.83, 123.01, 120.27, 59.86, 45.82, 43.71, 32.65, 24.43, 17.40.
Mass: 492.11(m/z).

3.3D. Synthesis of 4-methyl - N- (4-(4-oxo-2- ((2,2,3- trimethylcyclopent-3-en-1- yl)methyl)thiazolidin-3-yl)phenyl)benzenesulfonamide:
Pinkish-blue ppt, Melting point 449.89^{0}C, **^{1}H NMR (400 MHz,) in DMSO-d_6** δ 9.37 (1H, s), 8.09 (2H, d, J = 8.2 Hz), 7.24 (2H, d, J = 1.0 Hz), 7.14 (2H, d, J = 1.5 Hz), 7.10 (2H, d, J = 1.5 Hz), 5.89 – 5.86 (1H, m), 4.28-4.25(2H, m), 3.93 (2H,S), 1.89 – 1.85 (5H, m), 1.45 – 1.44 (2H, m), 1.42 – 1.41(1H,m), 0.97(3H, s) 0.80 (6H, s).
^{13} C NMR DMSO-400HZ: δ 166.11, 149.18, 134.88, 133.33,133.17, 132.37,132.47,129. 72, 129.03, 129.03, 123.80, 115.20, 58.65, 45.31, 43.69, 36.30, 29.73, 23.74, 20.24,17.49.
Mass: 471.27(m/z).

3.3E. Synthesis of 4-methoxy - N- (4-(4-oxo-2- ((2,2,3- trimethylcyclopent-3-en-1- yl)methyl)thiazolidin-3-yl)phenyl)benzenesulfonamide:
Pink-white ppt, Melting point 430.58^{o}C, **^{1}H NMR (400 MHz,) in DMSO-d_6** δ 9.37 (1H, s), 8.09 (2H, d, J = 8.2 Hz), 7.24 (2H, d, J = 1.0 Hz), 7.14 (2H, d, J = 1.5 Hz), 7.10 (2H, d, J = 1.5 Hz), 5.90 – 5.86 (1H, m), 4.29- 4.26(2H, m), 3.93 (2H,S),3.70 (3H, S) 1.88 – 1.85 (5H, m), 1.46 – 1.44 (2H, m),1.42 –1.41(1H m), 0.80 (6H, s).
^{13} C NMR DMSO-400HZ: δ157.40, 149.18, 134.88, 133.33, 133.17, 132.67, 132.47,125.
95 , 123.80, 115.20, 58.65, 54.46, 45.31, 43.69, 36.30, 29.73, 23.74, 20.24, 17.49.
Mass: 471.27(m/z).

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