RESEARCH ARTICLE

The Synthesis of Some New Heterocyclic compounds from Vanillin Derivatives

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ABSTRACT

This paper attempted to synthesize six heterocyclic compounds from vanillin derivatives (S1A, S1B, S1C, S2A, S2B, S2C) by reacting vanillin with succinic anhydride to obtain an ester (S). This ester was reacted with a primary amine as 2,4- Di-nitro-phenyl hydrazine and 4-chloroaniline to produce new Schiff bases. We performed an addition reaction with a C = N bond such as succinic anhydride and phthalic anhydride to produce heterocyclic compounds on these bases. Thin-layer chromatography (TLC) monitored these reactions, and then some physical properties such as melting point were measured and then diagnosed using Fourier-transform infrared spectroscopy (FTIR) and proton nuclear magnetic resonance (H-NMR) spectrum.

Keywords: Heterocyclic Compounds, Primary Amine, Schiff's bases, Succinic Anhydride, Vanillin derivatives.

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INTRODUCTION

Vanillin is an organic compound that can be obtained in extracts for many plants. Schiff's bases are products of reducing carbonyl compounds with primary amines and were first found by Schiff in 1864. A common compositional characteristic of these composites is the isomethenes group with the formula RHC= N-Rl, where R and Rl are alkyl, aryl, alkyl groups circular or heterocyclic groups which may be replaced. These composites are also known as emines or azomethines.[1]

Several studies have shown that the presence of the single electron pair in the sp2 hybrid orbit in the nitrogen atom of the azomethine group has great importance in biological and chemical effects. Because of the simplicity of preparation, the C = N group.[2,3]

Multiple diseases are increasing in the communities and constantly increasing the number of diseases resistant to multiple drugs and the emergence of strains of low response to antibiotics. It has given the intense mode of study for new antimicrobial materials. Schiff's bases are composites containing the C = N group. They are frequently synthesized from amine, aldehyde, or ketone. Schiff's rules have expanded importance due to their use in many pharmacological aspects such as anti-bacterial, anti-fungal, anti-reproductive, anti-tumor, and antipyretic. Schiff compound bases containing aryl substitutes are more stable and easy to manufacture.[4-6]

The chemistry of heterocyclic composites is one of the most crucial organic chemistry divisions due to the variety of its synthetic procedures and its industrial and physiological importance to heterocyclic compounds.[7-9] It has also been found that heterocyclic compounds are used in medicinal chemistry. It is mainly present in a large proportion of biomolecules such as enzymes, vitamins, and bioactive compounds that include anti-fungal and antimicrobials, antioxidant, anti-allergic, enzyme inhibitor, herbicide activity, and anti-cancer activity.[10-12]

SYNTHESIS

Synthesis of Vanillin Esterification (Compound S)

The preparation method was done by taking (0.06mol) of vanillin and placed in a round-bottomed vial, size 150mL with 100mL dioxanee, and then this round-bottomed was added (0.03 mol) of succinic anhydride. Now solution was reflux with stirred the next 8 to 9 hours at around 100–110°C. After reaction completion, the solvent was removed under reduced pressure by a rotatory evaporator. The obtained product was washed with diethyl ether to get a precipitated solid brown product (S).

Synthesis of Schiff Bases Ester

Schiff base (S1,S2) was prepared by using 0.04 mol of 4-bromoaniline, 2,4 dinatron-phenyl-hydrizene, respectively, and mixed with 0.02 mol of ester (compound S), and few drops of glacial acetic acid were added in a 150 mL round-bottomed flask was dissolved with (100 mL) ethanol, mixed solution stirred for (7, 9, 6, 8) hours, respectively at 90 to 110°C.

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The ethanol was removed under low pressure by a rotatory evaporator. A solid product was obtained, washed with ethanol, and filtered, dried, and melting point was taken. The melting point of compounds S1 and S2 are 168 and 189°C, respectively.

Synthesis of Heterocyclic compounds

Synthesis of Compound S1A

(0.002 mol) of compound S1 with (0.004 mol) of phthalic anhydride in a 150mL round-bottomed vial was dissolved with (100 mL) benzene, mixed solution stirred for (20 to 22) hours, at (80–110°C). Then the solvent was removed under low pressure by a rotatory evaporator and TLC monitored the mixture. The produce was gathered by recrystallization and filtration by ethanol. The melting point of compound S1A is 156°C

Synthesis of Compound S1B

A total of 0.002 mol of compound S1 with (0.004mol) of Sodium azide in a 150 mL round-bottomed vial was dissolved with (90 mL) dioxane, mixed solution stirred for 22-26 hours, at 100–110°C. the solvent was removed under low pressure by a rotatory evaporator. TLC monitored the mix. The produce was gathered by recrystallization and filtration by ethanol. The melting point of compound S1B is 165°C

Synthesis of Compound S1C

(0.002 mol) of compound S1 with (0.004 mol) maleic anhydride in a 150 mL round-bottomed vial was dissolved with (90 mL) dioxane, mixed solution stirred for 2 to 24 hours at 100 to 110°C. The solvent was removed under low pressure by a rotatory evaporator. TLC monitored the mix. The product was gathered by recrystallization and filtration by ethanol. The melting point of compound S1C is 70°C

Synthesis of Compound S2A

(0.002 mol) of compound S2 with (0.004 mol) of phthalic anhydride in a 150mL round-bottomed vial was dissolved with (100 mL) benzene, mixed solution stirred for 20 to 22 hours, at (80–110°C). The solvent was removed under low pressure by a rotatory evaporator. The mixture was monitored by TLC. The produce was gathered by recrystallized and filtration by ethanol.

Synthesis of Compound S2B

(0.002 mol) of compound S2 with (0.004 mol) of Sodium azide in a 150mL round-bottomed vial was dissolved with (90 mL) dioxane, mixed solution stirred for 22 to 26 hours, at (100–110°C). The solvent was removed under low pressure by a rotatory evaporator. TLC monitored the mixture. The product was collected by filtration and recrystallized by ethanol.

Synthesis of compound S2C

A total of 0.002 mol of compound S2 with (0.004 mol) of maleic anhydride in a 150mL round-bottomed vial was dissolved with (90 mL) dioxane, mixed solution stirred for 20 to 24 hours, at (100–110°C). The solvent was removed under low pressure by a rotatory evaporator. TLC monitored the mix. The produce was collected by filtration and recrystallized by ethanol.

Synthesis of Compound S2A

(0.00l mol) of compound S2 with (0.003 mol) of phthalic anhydride in a 100 mL round-bottomed vial was dissolved with (90 mL) benzene, mixed solution stirred for 20 to 22 hours, at (80–110°C). The solvent was removed under low pressure by a rotatory evaporator. TLC monitored the mix. The product was collected by filtration and recrystallized by ethanol.

RESULTS AND DISCUSSION

New compounds were obtained during the reaction of vanillin with succinic anhydride to obtain ester (S), as shown in Figure 1.

The compound was identified utilizing infrared spectroscopy, and the physical properties it was studied.

IR (KBr cm-1), (1240 (C-O-C Str, ether), 3085 (C-H, Ar-H Str), 1220 (C-O Str), 1741 (C=O Str, ester group), 1704 (C=O Str, aldehyde group); 1HNMR

Two new compounds were obtained during the reaction of ester vanillin derivative (S) with primary amine such as 4-bromoaniline, 2,4 dinitrophenylhydrazene to obtain schiff base (S1 and S2), respectively, as shown in Figure 2.

Infrared spectroscopy identified the compound by the disappearance of first amine group at (3500-3600cm^{-1}) and the appearance of imine (C=N) at (1660, 1540 cm^{-1}). Its physical properties were studied as melting point (m.p.) of S1=1700C and S2=183°C.

A reaction was performed in addition to the double bond in the two compounds prepared above to obtain 6 new heterocyclic compounds through the interaction of the above prepared Schiff bases with sodium azide, as well as phthalic anhydride and maleic anhydride, as Figure 3.

The above-prepared compounds were identified by the H-NMR spectrum, whereas the resonance of protons in the composites was determined based on their multiplicity and integration pattern. The 1H-NMR spectra of the Schiff bases in DMSO exhibit signals at 9.1, 9.30, and 9.35 ppm for compounds S1B, S2C, and S2A, attributed to CH=N- protons, respectively.

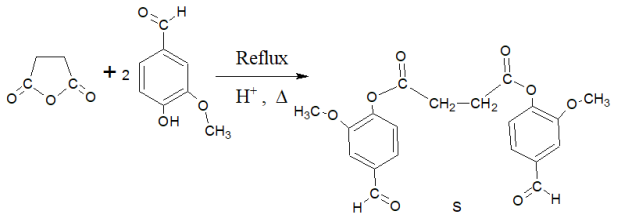

Figure 1: Represents a method for preparing duo ester

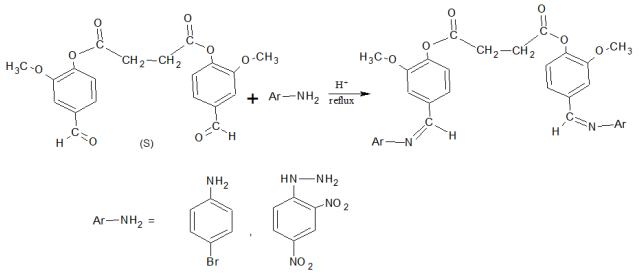

Figure 2: Representing a method for preparing Schiff bases.

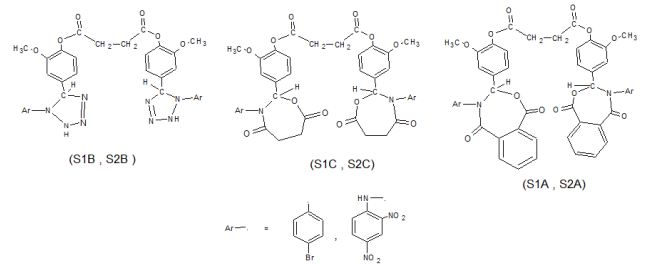

Figure 3: Representing heterocyclic compounds

CONCLUSION

The two components of the two Schiff bases were prepared as raw materials for the preparation of six heterocyclic compounds that contain an atom of nitrogen or oxygen through the addition reaction process, and we expect the compounds prepared to have antibacterial activity.

REFERENCES

1. Norrihan S, Md Abu A, Md Abdus S, Fasihuddin B A, Mohd Razip A. Synthesis, spectral characterization and biological activities of Organotin (IV) complexes with ortho-vanillin-2-hydrazinopyridine (VHP). Open Journal of Inorganic Chemistry. 2012 Apr 24;2012.
2. Sinha D, Tiwari AK, Singh S, Shukla G, Mishra P, Chandra H, Mishra AK. Synthesis, characterization and biological activity of Schiff base analogues of indole-3-carboxaldehyde. European journal of medicinal chemistry. 2008 Jan 1;43(1): 160-165.
3. Chigurupati S. Designing new vanillin schiff bases and their antibacterial Studies. J Med Bioeng 2015; 4: 363-366.
4. Amin RM, Abdel-Kader NS, El-Ansary AL. Microplate assay for screening the antibacterial activity of Schiff bases derived from substituted benzopyran-4-one. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2012 Sep 1;95:517-525.
5. Neelakantan MA, Esakkiammal M, Mariappan SS, Dharmaraja J, Jeyakumar T. Synthesis, characterization and biocidal activities of some schiff base metal complexes. Indian Journal of Pharmaceutical Sciences. 2010 Mar;72(2):216.
6. Kumar J, Rai A, Raj V. A comprehensive review on the pharmacological activity of schiff base containing derivatives. Org Med Chem J. 2017;1:555-564
7. Al-Juburi RM. Synthesis and characterization of some heterocyclic compounds (oxazepine, tetrazole) derived from Schiff bases. Al-Nahrain Journal of Science. 2012;15(4):60-67.
8. Caiazzo A, Dalili S, Picard C, Sasaki M, Siu T, Yudin AK. New methods for the synthesis of heterocyclic compounds. Pure and applied chemistry. 2004 Jan 1;76(3):603-613.
9. Al-Mulla A. A review: biological importance of heterocyclic compounds. Der Pharma Chemica. 2017;9(13):141-147.
10. Xavier A, Srividhya N. Synthesis and study of Schiff base ligands. IOSR Journal of Applied Chemistry. 2014 Nov;7(11):06-15.
11. Brodowska K, Lodyga-Chruscinska E. Schiff bases—interesting range of applications in various fields of science. ChemInform. 2015 Mar;46(11).
12. Aenugu HP, Kumar DS, Srisudharson NP, Ghosh SS, Banji D. International Journal of ChemTech Research CODEN. InIJCRGG 2011 Apr (Vol. 3, No. 2, pp. 825-836)..