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RESEARCH ARTICLE

GREEN SYNTHESIS OF SOME NOVEL N-MANNICH BASES USING ENVIRONMENTALLY BENIGN CATALYST UNDER SOLVENT FREE CONDITIONS

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ABSTRACT

The present research article describes the synthesis of N-Mannich bases of 3, 4-dihydropyrimidin-2 (1H)-ones (DHPMs) using Ethylene di ammonium diacetate (EDDA) as catalyst. The heterocyclic precursor DHPMs were synthesized by Bignelli reaction of aromatic aldehyde, ethyl acetoacetate and urea using ionic liquid. Three series of N-Mannich bases have been synthesized by Mannich reaction of 3, 4-dihydropyrimidin-2(1H)-one with different heterocyclic secondary amines namely morpholine, piperazine tetrahydrocarbazole, diethanolamine, imidazole and formaldehyde. The products of Mannich reactions have been characterized by elemental and spectral studies. The results indicated that the catalyst EDDA exhibited excellent catalytic activity for the Mannich condensation and better yield (with high degree of purity) under mild reaction conditions than those reactions with conventional catalyst. In conclusion the present method is a very efficient and selective protocol for Mannich condensation reactions of DHPMs (Bignelli compounds) in the presence of reversible and environmentally benign catalyst. Simple work-up procedure, solvent less condition is another advantage of this method.

INTRODUCTION

Organic synthesis generally required large amount of solvent, avoiding the use of organic solvents in synthesis is a paradigm shift directed at developing more benign chemistry, and with ionic liquids surprisingly can lead to access to new compounds (Zhang Gao *et al.,* 2005). In recent years, environmentally-friendly reaction processes have vigorously been studied from the stand point of green chemistry (Rajendran, 2010). For example, Oxidation reactions with the air, or reaction in water, supercritical fluids, and fluorous solvents are cited (Larock, 1999). Most recently, ionic liquids have gained much attention as green solvents for organic synthesis (Shelton *et al.,* 2009). The Mannich reaction as a powerful C-C bond formation process has wide application for the preparation of diverse amino alkyl derivatives. It involves the condensation of a compound capable of supplying one or more active hydrogen

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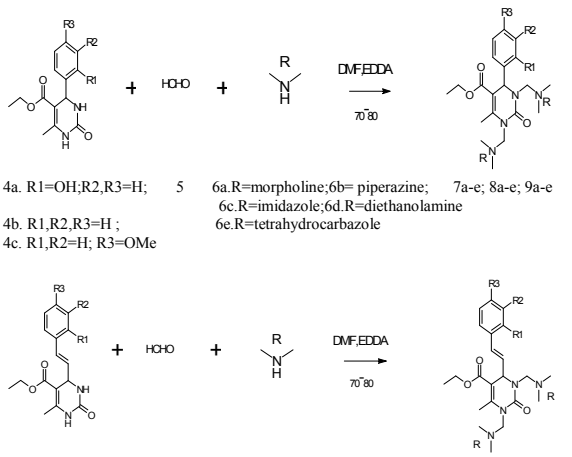
atoms with aldehyde and primary or secondary amine (Smith and March, 2001). Mannich bases are physiologically reactive because of the function rendering the molecule soluble in aqueous solvent when it is transformed into ammonium salt. Further, a considerable amount of work has been reported on the synthesis and pharmacological activity of various Mannich bases for analgesic, antispasmodic, anesthetic and antimicrobial activity as well as intermediates in drug synthesis (Jay *et al.,* 2010). In this context, literature survey has revealed a number of reports on antimicrobial activity of N-Mannich bases derived from different heterocyles such as pyrrole, pyrazole, benzimidazole, Benzotriazole, etc., Shah *et al* have carried out Mannich reaction of five membered heterocyclic ring systems with HCHO and primary or secondary amines and the resulting compounds have been tested for antibacterial antifungal, antiviral, anticancer, antileishmanial and antimalarial activity (Shah *et al.,* 2010). Keeping in view of the importance of these two organic moieties, DHPMs and N-Mannich base in the field of medicine and biology, an attempt has now been made to synthesis N-Mannich base containing both the moieties by using EDDA as catalyst (Vasundhara Singh *et al.,* 2010).

MATERIAL AND METHODS

Chemicals

All the chemicals were purchased from Aldrich chem. All liquid reagents were distilled before use. Imidazole, diethanolamine, morpholine, piperazine were purchased from Aldrich chem. General procedure for the synthesis of N-Mannich bases: 7a-e; 8a-e and 9a-e Preparation of ethyl 1,3-morpholine-1-yl - methyl - 4- (2-hydroxy-phenyl) – 6 – methyl – 2 – oxo - 1, 2, 3, 4- tetrahydro – 5 - pyrimidinde carboxylate 7a-e.

To a solution of DHPM 4a (0.1mole) in DMF, formaldehyde 5 (0.2 mole) were added under stirring. The reaction mixture was stirred at RT for 0.5 hr to complete the reaction of formaldehyde and to yield methylol derivative of 4a. To this, a solution of 6a (0.2 mole in DMF was added drop wise and EDDA catalyst (0.2 mole) was added into it. It was refluxed for one hour. The reaction mixture was poured into ice cold water and filtered off and washed with hot water (Shah *et al.,* 2009). Finally, it was dried and purified by recrystallization from chloroform to give 7a (Scheme-1). In a similar way, the remaining two series of N-Mannich bases 8a-e, 9a-e have been prepared by Mannich reaction of DHPMs 4b and 4c with the five heterocyclic secondary amines 6a-e and formaldehyde 5 in presence of EDDA as catalyst (Shelke *et al.,* 2009). The analytical data and spectral studies of these three series of N-Mannich bases are furnished (Sahoo *et al.,* 2006).



Scheme1. Synthesis of N-Mannich bases: 7a-e; 8a-e and 9a-e

Elemental analysis and spectral characterization of the products

Elemental analyses were carried out on a Perkin Elmer auto analyzer. Melting point of Mannich bases were determined by open capillary method and are uncorrected (Ganeshpure *et al.,* 2007). Infra Red absorption spectra (IR) were scanned on a Nicolet-400D FT-IR spectrophotometer using KBr pellets and ^{1}H-NMR spectra were scanned in $CDCl_3$ on Bruker AC-90 MHz FT-NMR instrument using TMS as an internal standard. Spectral characteristics of the products are presented in Appendix-1.

Appendix -1

Spectral characterization data of N-Mannich bases 7a-e, 8a-e, 9a-e

7a. *^{1}H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 2.66(s) 2H,-CH_2 of morpholine ring adjacent to adjacent to nitrogen; 3.56(s) 2H, -CH_2 of morpholine ring adjacent to oxygen; 9.01(s) 1H, -OH of phenyl ring present in Bignelli compound; 6.7-7.2 (m)4H, one aromatic rings*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d), 153.99(s),130. 04(d), 120.96(s), 117.71(d), 127.52(d), 53.34(d), 148.85(s), 101.34(s), 148.54(s), 167.74(s), 60.96(t),13.95(q)17.57(q), 62.19(t), 45(t), 63.24(t), 58.8(t), 63.24(t), 58.8(t), 58.8(t), 58.8(t), 58.8(t), 58.8(t)

7b.*^{1}H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 2.66(t) 2H,-CH_2 of piperazine ring adjacent to nitrogen; 9.01(s) 1H, -OH of phenyl ring present in Bignelli compound; 6.7-7.2 (m)4H, one aromatic rings; 4.12(s) 1H of amino group*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d), 151.99(s), 134.04(d), 120.86(s), 117.61(d), 126.82(d), 52.94(d), 147.95(s), 101.45(s), 148.64(s), 168.14(s), 60.92(t),13.89q)17.57(q), 62.19(t), 44.98(t), 63.24(t), 57.8(t), 63.24(t), 57.8(t), 59.24(t), 58.8(t), 59.4(t), 57.89 (t)

7c. *^{1}H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 8.00(s) 1H,-CH of imidazole ring 9.01(s) 1H, -OH of phenyl ring present in Bignelli compound; 6.7-7.2 (m)4H, one aromatic ring;5.25(d) 2H, -CH of imidazole ring*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d), 154.88(s),130.04(d),120.96(s),117.71(d), 128.42(d), 53.9(d), 148.85(s), 101.34(s),149.85(s), 167.74(s), 60.96(t), 13.95(q), 17.57(q), 53.65(t), 42.44(t), 133.11(s), 143.85(s), 142.42(s), 133.85(s), 147.43(s), 156.91(s),

7d. *^{1}H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH3 of ester group; 2.31(s) 3H,-CH3 of pyrimidine ring; 4.00(q) 2H, -CH2 of ester group; 4.22(s) 2H, -CH2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 9.01(s) 1H, -OH of phenyl ring present in Bignelli compound; 6.7-7.2 (m)4H, one aromatic ring; 1.5(t) 2H,CH2 attached to amino methyl group; 2.5(t) 2H, -CH2 group adjacent to amino group, 3.7(t),2H,CH2 group adjacent to OH group*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d),154.72(s),130.04(d), 121.94(s), 117.71(d), 127.26(d), 54.2 (d),147.95(s), 103.29(s), 146.17(s), 60.96(t), 53.66(t), 42.44(t), 28.3(t), 47.00(t), 62.19(t), 63.24(t), 58.8(t), 53.65(t), 42.09(t), 33.51(t), 17.57(q), 13.95(q)

7e. *^{1}H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH3 of ester group; 2.31(s) 3H,-CH3 of pyrimidine ring; 4.00(q) 2H, -CH2 of ester group; 4.22(s) 2H, -CH2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 9.01(s) 1H, -OH of phenyl ring present in Bignelli compound; 7.0-7.6(m)12H, three aromatic rings; 2.64(q) 2H, -CH2 of carbazole ring adjacent to double bond; 1.89(q) 2H,-CH2 of carbazole ring*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d),154.76(s), 130.04(d), 121.44(s), 117.71(d), 127.30(d), 55.26(d), 148.85(s), 100.36(s), 149.85(s), 167.74(s), 60.96(t), 13.95(q),17.7(q), 57.2(t), 42.89(t), 132.91(s), 93.09(s), 137.7(s), 125.51(s), 135.57(s), 93.96(s), 138.04(s), 128.94(s), 111.7(d), 121.26(d), 118.49(d), 119.09(d), 21.38(t), 22.99(t), 22.25(t), 22.99(t), 20.45(t), 22.99(t), 22.25(t), 22.99(t), 108.12(d), 121.53(d), 118.75(d), 118.37(d)

8a. *^{1}H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 2.66(s) 2H,-CH_2 of morpholine ring adjacent to adjacent to nitrogen; 3.56(s) 2H, -CH_2 of morpholine ring adjacent to oxygen; 7.4(s)5H, one aromatic ring;7.42(d)1H, -CH of vinylic proton placed on unsaturated carbonyl system; 6.6(dd) 2H, alkenic proton*

^{13}C NMR (90MHz, dmso-d_6)

113.22(d), 131.44(s), 160.15(d), 129.93(s), 113.22(d), 131.14(d), 61.9(d), 148.85(s), 100.36(s), 148.54(s), 100.36s), 148.54(t),167.74 (s)17.57(q), 60.96(t), 13.95(q)17.57(q), 62.19(t),55.2(q), 58.8(t), 58.8(t), 58.8(t), 58.8(t), 58.8(t), 63.24(t),61.54(t)

8b.*[1]H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 2.66(t) 2H,-CH_2 of piperazine ring adjacent to nitrogen compound;; 4.12(s) 1H of amino group; 7.4(s)5H, one aromatic ring;7.42(d)1H, -CH of vinylic proton placed on unsaturated carbonyl system; 6.6(dd) 2H, alkenic proton*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d), 151.99(s), 134.04(d), 120.86(s), 117.61(d), 126.82(d), 131.14(d), 52.94(d), 148.64(s), 168.14(s), 60.92(t),13.89q)17.57(q), 62.19(t), 44.98(t), 63.24(t), 57.8(t), 63.24(t), 57.8(t), 59.24(t), 58.8(t), 59.4(t), 57.89 (t), 150.7(d), 143.7(d),62.65 (d)

8c. *[1]H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 8.00(s) 1H,-CH of imidazole ring; 5.25(d) 1H, -CH of imidazole ring;7.4(s)5H, one aromatic ring;7.42(d)1H, -CH of vinylic proton placed on unsaturated carbonyl system; 6.6(dd) 2H, alkenic proton*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d), 154.88(s),130.04(d), 120.96(s),117.71(d), 128.42(d), 53.48(d), 107.3(d), 120.29(d),120.47(d), 65.97(d), 134.58(d), 124.92(d),110.92(d), 60.96(t), 53.65(t),53.31(t),17.57(q),13.95(q), 167.74(s), 143.85(s), 126.06(d), 128.8(d), 120.84(d)

8d. *[1]H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 7.4(s) 5H, one aromatic ring; 2.5(t) 2H, -CH_2 group adjacent to amino group, 3.7(t),2H,CH_2 group adjacent to OH group; 4.5(s) 1H, -OH of aliphatic alcohol;7.4(s)5H, one aromatic ring;7.42(d)1H, -CH of vinylic proton placed on unsaturated carbonyl system; 6.6(dd) 2H, alkenic proton*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d), 156.2(s), 148.85(s), 167.74(s), 133.49(s), 117.71(d), 129.74(d), 50.09(d), 134.58(d),127.26(d), 120.84(d), 121.62(d),42.44(t), 60.96(t), 58.8(t), 63.24(t), 62.19(t),42.09(t), 61.45(t), 13.95(q), 17.57(q)

8e. *[1]H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 7.0-7.6(m)12H, three aromatic rings; 2.64(q) 2H, -CH_2 of carbazole ring adjacent to double bond; 1.89(q) 2H,-CH_2 of carbazole ring; 7.4(s)5H, one aromatic ring;7.42(d)1H, -CH of vinylic proton placed on unsaturated carbonyl system; 6.6(dd) 2H, alkenic proton*
[13]C NMR (90MHz, dmso-d_6)

116.21(d), 130.9(d), 160.15(s),130.47(s), 113.22(d), 130.91(d), 62.61(d), 148.85(s), 100.36(s), 60.96(t), 13.95(q), 17.57(q), 57.2(t), 55.2(q), 42.89(t), 137.3(s), 125.51(s), 132.91(s), 93.09(s), 93.96(s), 135.57(s), 128.97(s), 138.04(s), 118.49(d), 119.09(d), 111.78(d), 121.26(d) 22.25(t), 22.99(t), 21.38(t), 22.99(t), 108.12(d), 121.58(d),118.75(d), 118.37(d), 20.42(t), 22.99(t), 22.25(t), 22.99(t)

9a. *[1]H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 2.66(s) 2H,-CH_2 of morpholine ring adjacent to adjacent to nitrogen; 3.56(s) 2H, -CH_2 of morpholine ring adjacent to oxygen; 3.78(s) 3H, -OCH_3 of phenyl ring present in Bignelli compound; 6.7-7.2 (m)4H, one aromatic rings*

^{13}C NMR (90MHz, dmso-d_6)

113.22(d),131.14(d), 160.15(s), 120.93(s), 113.22(d), 131.14(d), 61.9(d), 148.85(s), 100.36(s), 148.54(s), 167.74(s), 60.96(t), 13.95(q), 17.57(q), 62.19(t), 55.2(q), 61.54(t), 58.8(t), 63.24(t), 58.8(t), 63.24(t), 58.8(t), 58.8(t), 58.8(t), 58.8(t)

9b.*[1]H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 7.05(s) 1H, H on pyrimidine ring; 2.66(t) 2H,-CH_2 of piperazine ring adjacent to nitrogen compound;; 4.12(s) 1H of amino group; 6.7-7.2 (m)4H, one aromatic rings; 3.78(s) 3H, -OCH_3 of phenyl ring present in Bignelli compound*

^{13}C NMR (90MHz, dmso-d_6)

113.22(d),130.14(d), 160.15(s), 129.93(s), 113.22(d), 130.91(d), 62.61(d), 148.85(s), 100.36(s), 146.34(s), 167.74(s), 60.96(t), 13.95(q), 17.57(q), 62.19(t), 57.2(q), 62.65(t), 58.8(t), 63.24(t), 58.8(t), 63.24(t), 55.9(t), 58.8(t), 58.8(t), 58.8(t)

9c. *[1]H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl*

bridge; 6.66(s) 1H, H on pyrimidine ring; 8.00(s) 1H,-CH of imidazole ring; 5.25(d) 1H, -CH of imidazole ring; 6.7-7.2 (m)4H, one aromatic rings; 3.78(s) 3H, -OCH_3 of phenyl ring present in Bignelli compound;
^{13}C NMR (90MHz, dmso-d_6)

113.21(d),132.03(d), 160.15(s), 126.32(s), 113.22(d), 132.03(d), 61.46(d), 148.85(s), 100.36(s), 149.85(s), 167.74(s), 60.96(t), 13.95(q), 17.57(q), 47.88(t), 43.98(t), 132.66(s), 140.73(s), 132.32(d), 133.4(s), 144.34(s), 143.5(d), 110.74(d), 122.3(d), 119.8(d), 121.0(d)107.13(d), 122.56(d), 120.06(d), 120.29(d), 55.2(q)

9d. *^{1}H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 6.7-7.2(m) 4H, one aromatic ring; 2.5(t) 2H, -CH_2 group adjacent to amino group, 3.7(t),2H,CH_2 group adjacent to OH group; 4.5(s) 1H, -OH of aliphatic alcohol; 3.78(s) 3H, -OCH_3 of phenyl ring present in Bignelli compound;*

^{13}C NMR (90MHz, dmso-d_6)

116.21(d), 156.2(s), 148.85(s), 167.74(s), 133.49(s), 117.71(d), 129.74(d), 50.09(d), 134.58(d),127.26(d), 120.84(d), 121.62(d),42.44(t), 60.96(t), 58.8(t), 63.24(t), 62.19(t),42.09(t), 61.45(t), 13.95(q), 17.57(q)

9e. *^{1}H-NMR (200 MHz, $CDCl_3$) 1.20(t) 3H,-CH_3 of ester group; 2.31(s) 3H,-CH_3 of pyrimidine ring; 4.00(q) 2H, -CH_2 of ester group; 4.22(s) 2H, -CH_2 of amino methyl bridge; 6.66(s) 1H, H on pyrimidine ring; 7.0-7.6(m)12H, three aromatic rings; 2.64(q) 2H, -CH_2 of carbazole ring adjacent to double bond; 1.89(q) 2H,-CH_2 of carbazole ring; 3.78(s) 3H, -OCH_3 of phenyl ring present in Bignelli compound;*

^{13}C NMR (90MHz, dmso-d_6)

113.22(d), 130.91(d), 160.15(s), 130.47(s), 113.22(d), 130.91(d),62.61(d), 148.85(s), 100.36(s), 146.34(s), 167.74(s), 60.96(t), 13.95(q), 17.57(q), 57.2(t), 55.2(q), 42.89(t), 137.3(s), 125.51(s), 132.91(s), 93.09(s), 93.96(s), 135.57(s), 129,97(s), 138.04(s), 118.49(d), 119,09(d), 111.78(d), 121.26(d), 22.25(t0, 22.99(t), 21.38(t), 22.99(t), 108.12(d), 121`.58(d), 118.75(d), 118.37(d), 20.42(t), 22.99(t0, 22.25(t), 22.99(t)

RESULTS AND DISCUSSION

The present paper describes the synthesis of three series of novel N-Mannich bases of DHPMs using EDDA as catalyst. These series of N-Mannich bases have been synthesized by Mannich reaction of 3, 4-dihydropyrimidin-2(1H)-one with different heterocyclic secondary amines namely morpholine, piperazine tetrahydrocarbazole, diethanolamine, imidazole and formaldehyde (Scheme 1). All three DHPMs substrate and their N-Mannich bases have been characterized by elemental and spectral studies. When the Mannich condensation reactions were carried out with the proposed catalyst EDDA it was found that greater % of yield, high degree purity of the products, low reaction temperature (low thermal energy), less reaction time than those of conventional reactions (without catalyst). Results are presented in Table 1.

Table1. Results of Mannich condensation reactions with the proposed catalyst and without catalyst (conventional reaction)

Compounds	Time(min)	Time(min) in Conventional reaction	Temp(^{o}C)	Temp(^{o}C) of Conventional reaction	(%)Yield	(%)Yield of Conventional reaction
7a	60	120	75	110	85	81
7b	50	120	70	115	80	76
7c	50	120	80	110	85	81
7d	60	120	75	110	76	75
7e	90	120	70	110	84	84
8a	60	120	75	110	78	76
8b	55	120	80	115	75	71
8c	60	120	70	110	80	78
8d	70	120	75	110	85	82
8e	80	120	85	110	83	87
9a	70	120	70	110	89	86
9b	50	120	75	115	74	71
9c	50	120	80	115	80	79
9d	60	120	75	110	86	80
9e	90	120	70	115	80	77

secondary amino components 1H NMR spectra of o

Table 2. Analytical characterization data of N-Mannich bases 7a-e, 8a-e and 9a-e

Compound	m.p ^{o}C	Mol. Formula	Calcd. (%) (Found)		
			C	H	N
7a	204	$C_{24}H_{34}N_4O_6$	60.75(60.44)	7.23(7.53)	11.81(11.38)
7b	201	$C_{24}H_{36}N_6O_4$	61.01(61.40)	7.62(7.56)	17.79(17.69)
7c	189	$C_{22}H_{24}N_6O_4$	60.55(60.45)	5.50(5.28)	19.26(19.21)
7d	222	$C_{24}H_{38}N_4O_8$	56.47(56.43)	7.45(7.42)	10.98(10.90)
7e	255	$C_{40}H_{41}N_4O_4$	74.88(74.83)	6.39(6.34)	8.73(8.70)
8a	215	$C_{26}H_{36}N_4O_5$	60.75(60.34)	7.17(7.12)	11.81(11.62)
8b	195	$C_{26}H_{40}N_6O_3$	61.01(61.13)	7.62(7.52)	17.79(17.69)
8c	201	$C_{24}H_{26}N_6O_3$	60.55(60.33)	5.50(5.54)	19.26(19.35)
8d	230	$C_{26}H_{40}N_4O_7$	56.47(56.40)	7.45(7.38)	10.98(10.85)
8e	242	$C_{42}H_{44}N_4O_3$	74.76(74.71)	6.54(6.48)	8.72(8.74)
9a	238	$C_{24}H_{34}N_4O_6$	64.46(64.39)	7.43(7.38)	11.57(11.48)
9b	236	$C_{24}H_{36}N_6O_4$	64.46(64.41)	8.26(8.13)	17.35(17.26)
9c	228	$C_{22}H_{24}N_6O_4$	64.57(64.50)	5.82(5.76)	18.83(18.78)
9d	214	$C_{24}H_{38}N_4O_8$	60.00(60.15)	7.69(7.61)	10.76(10.71)
9e	252	$C_{40}H_{42}N_4O_4$	77.30(77.15)	6.74(6.63)	8.58(8.21)

Synthesis of N-Mannich bases based on these DHPMS substrate resulted in three series of N-Mannich bases7a-e;8a-e;9a-e; with yield (70-90%) examination of analytical (Table 2) and spectral data of all the N-Mannich bases (Appendix 1) are in good agreement with calculated values based on proposed structure shown in Scheme1. When EDDA is used as catalyst even at the temperature lower than that of the conventional reaction, products are formed in better yield.

Spectral studies of N-Mannich bases have shown the following characteristic absorption bands of DHPMs component in IR spectra of N-Mannich bases resemble the pattern observed for parent DHPMs substrate reported in Experimental Section with the exception that the absorption bands at 1550 and 700 cm-1 due to secondary (-NH) group of DHPM substrate disappeared in the IR spectra of each of the N-Mannich bases. Two strong band respectively the region 2780-2770 and 1430-1420 cm^{-1} are due to –CH stretching and bending vibration of two methylene linkages between DHPMs substrate and two heterocyclic (1H,-NH) singlet of secondary amino groups of DHPMs ring systems. This suggests that the hydrogen atom of two secondary amino groups have reacted with formaldehyde and heterocyclic amino compounds to form disubstituted N-Mannich base. This can be further confirmed from the appearance of two new ^{1}H NMR signals in the range of 4.20-6.10 and 4.80-6.90 values due to ($2H,–CH_2$) of methylene linkage formed between DHPMs strong bands in the region of 1750-1690 cm^{-1} represent the –C=O stretching vibration of the conjugated ester. All these inferences support the predicted chemical structure of some novel N-Mannich bases shown in Scheme 1.

Conclusion

The heterocyclic N-Mannich bases prepared from DHPMs in presence of EDDA catalyst at low temperature than that of the conventional reactions and the product formed is in better yield. Operational simplicity, mild reaction conditions, environment and eco - friendly, compatibility with various functional groups, high yields and

reagents as catalyst are the advantages of the present methodology for the synthesis of dihydropyrimidinones.

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