An efficient and eco-friendly synthesis of 1,4-dihydropyridines via Hantzsch reaction in Glycine-HCl buffer as solvent and bio-catalyst

Ali Reza Molla Ebrahimlo*, Mounes Hanaforoush and Roya Attari

Department of Chemistry, Islamic Azad University, Khoy Branch, P.O. Box 58168–44799, Khoy, Iran

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Figure S1: $^1$H NMR (CDCl$_3$, 300 MHz) spectrum of compound 3a

Figure S2: $^1$H NMR (CDCl$_3$, 300 MHz) spectrum of compound 3b

Figure S3: $^1$H NMR (CDCl$_3$, 300 MHz) spectrum of compound 3d

Figure S4: $^1$H NMR (CDCl$_3$, 300 MHz) spectrum of compound 3e

Figure S5: $^1$H NMR (CDCl$_3$, 300 MHz) spectrum of compound 3f

Figure S6: $^1$H NMR (CDCl$_3$, 300 MHz) spectrum of compound 3g

Figure S7: $^1$H NMR (CDCl$_3$, 300 MHz) spectrum of compound 3i

Figure S8: $^1$H NMR (CDCl$_3$, 300 MHz) spectrum of compound 3j
S1: Preparation of Glycine buffers:

a) Glycine- HCl buffer (pH=2.2)
50mL of 0.2M solution of Glycine (15.01g in 1L) is added to 44 mL of 0.2M solution of HCl and then is diluted to a volume of 200 mL.

b) Glycine- HCl buffer (pH=3)
50mL of 0.2M solution of Glycine (15.01g in 1L) is added to 11.4 mL of 0.2M solution of HCl and then is diluted to a volume of 200 mL.

c) Glycine- HCl buffer (pH=3.6)
50mL of 0.2M solution of Glycine (15.01g in 1L) is added to 3.6 mL of 0.2M solution of HCl and then is diluted to a volume of 200 mL.

d) Glycine- NaOH buffer (pH=9)
50mL of 0.2M solution of Glycine (15.01g in 1L) is added to 8.8 mL of 0.2M solution of NaOH and then is diluted to a volume of 200 mL.

e) Glycine- NaOH buffer (pH=10)
50mL of 0.2M solution of Glycine (15.01g in 1L) is added to 32 mL of 0.2M solution of NaOH and then is diluted to a volume of 200 mL.

S2: General procedure for the one-pot Hantzsch reaction in buffer solution:

A mixture of aldehyde (1 mmol), alkyl acetoacetate (2 mmol) and anhydrous ammonium carbonate (1 mmol) was stirred in buffer solution (pH=2.2, 3 mL) at 50–65 °C. After completion of the reaction (TLC monitoring), the mixture was diluted with cold H2O (5 mL) and filtered to remove the precipitated product which was further purified by recrystallization from EtOH/H2O.

S3: HNMR data for selected compounds:

Entry 3a: White crystals, m.p.: 154-157°C (Lit1:156-157), HNMR (400 MHz, CDCl3): 1.22 (t, 6H, J=7.1 Hz), 2.33(s, 6H), 4.08 (q, 4H, J=7.1 Hz), 4.98 (s, 1H), 5.59 (brs,1H), 7.10–7.29 (m, 5H); 3d: Yellows crystals, 129-131°C (Lit2:128-130), HNMR (300 MHz, CDCl3): 1.22 (t, 6H, J=7.1 Hz), 2.31(s, 6H), 4.08 (q, 4H, J=7.1 Hz), 4.95 (s, 1H), 5.89 (brs,1H), 7.16 (d, 2H, J=8.5 Hz), 7.21 (d, 2H, J=8.5 Hz); 3e: Orange crystals, 144-145°C (Lit3:145-146), HNMR (300 MHz, CDCl3): δ(HNMR δ(ppm): 1.23(t, J=7.09Hz , 6H) , 2.35(s, 6H), 3.64(s, 6H), 4.96(s, 1H), 5.75 (brs,1H), 7.02(d, 2H, J=7.90 Hz), 7.15(d, 2H, J=8.04 Hz); 3j: Yellow crystals 195-198°C (Lit4:196-198), HNMR (300 MHz, CDCl3): 2.36 (s, 6H), 3.64 (s, 6H), 5.10 (s, 1H), 5.85 (brs, 1H), 7.43(d, 2H, J=8.73 Hz), 8.08(d, 2H, J=8.73 Hz).

References


Figure S1: $^1$H NMR (CDCl₃, 400 MHz) spectrum of diethyl 4-(4-phenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(3a)
Figure S2: $^1$H NMR (CDCl$_3$, 400 MHz) spectrum of diethyl 4-(4-methylphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(3b)
Figure S3: $^1$H NMR (CDCl$_3$, 400 MHz) spectrum of diethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(3d)
Figure S4: $^1$H NMR (CDCl$_3$, 400 MHz) spectrum of diethyl 4-(4-nitrophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(3e)
Figure S5 : $^1$H NMR (CDCl$_3$, 400 MHz) spectrum of dimethyl 4-(4-phenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5 dicarboxylate(3f)
Figure S6: $^1$H NMR (CDCl$_3$, 400 MHz) spectrum of dimethyl 4-(4-methylphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(3g)
Figure S7: $^1$H NMR (CDCl$_3$, 400 MHz) spectrum of dimethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(3i)
Figure S8: $^1$H NMR (CDCl$_3$, 400 MHz) spectrum of dimethyl 4-(4-nitrophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(3j)