Supporting Information

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

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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 H_2O (5 mL) and filtered to remove the precipitated product which was further purified by recrystallization from $EtOH/H_2O$.

S3: HNMR data for selected compounds:

Entry **3a**: White crystals, m.p. : 154-157°C (Lit[1]:156-157), HNMR (400 MHz, $CDCl_3$): 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 (Lit[2]:128-130), HNMR (300 MHz, $CDCl_3$): 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 (Lit[1]:145-146), HNMR (300 MHz, $CDCl_3$): ^{1}HNMR δ(ppm): 1.23(t, J=7.09Hz , 6H) , 2.35(s, 6H) , 4.09(q, J=7.16Hz , 4H) , 5.09(s, 1H) , 6.05(bs, 1H) , 7.46(d, J=8.7Hz , 2H) , 8.08(d, J=8.7Hz 2H); **3g**: Orange crystals, 174-176°C (Lit[3]:175-177), HNMR (300 MHz, $CDCl_3$): 2.27(s, 3H), 2.32(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 (Lit[4]:196-198), HNMR (300 MHz, $CDCl_3$): 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).

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[2] Berson, J. A.; Brown, E., Studies on Dihydropyridines. I. The preparation of unsymmetrical 4-Aryl-1,4-dihydropyridines by the Hantzsch-Beyer synthesis. *J. Am. Chem. Soc.* **1955**, *77*, 444-447.

[3] Sivamurugan, V.; Vinu, A.; Palnichamy, M.; Murugesan, V. Rapid and cleaner synthesis of 1,4-dihydropyridines in aqueous medium. *Heteroat. Chem.* **2006**, *17*, 267-271.

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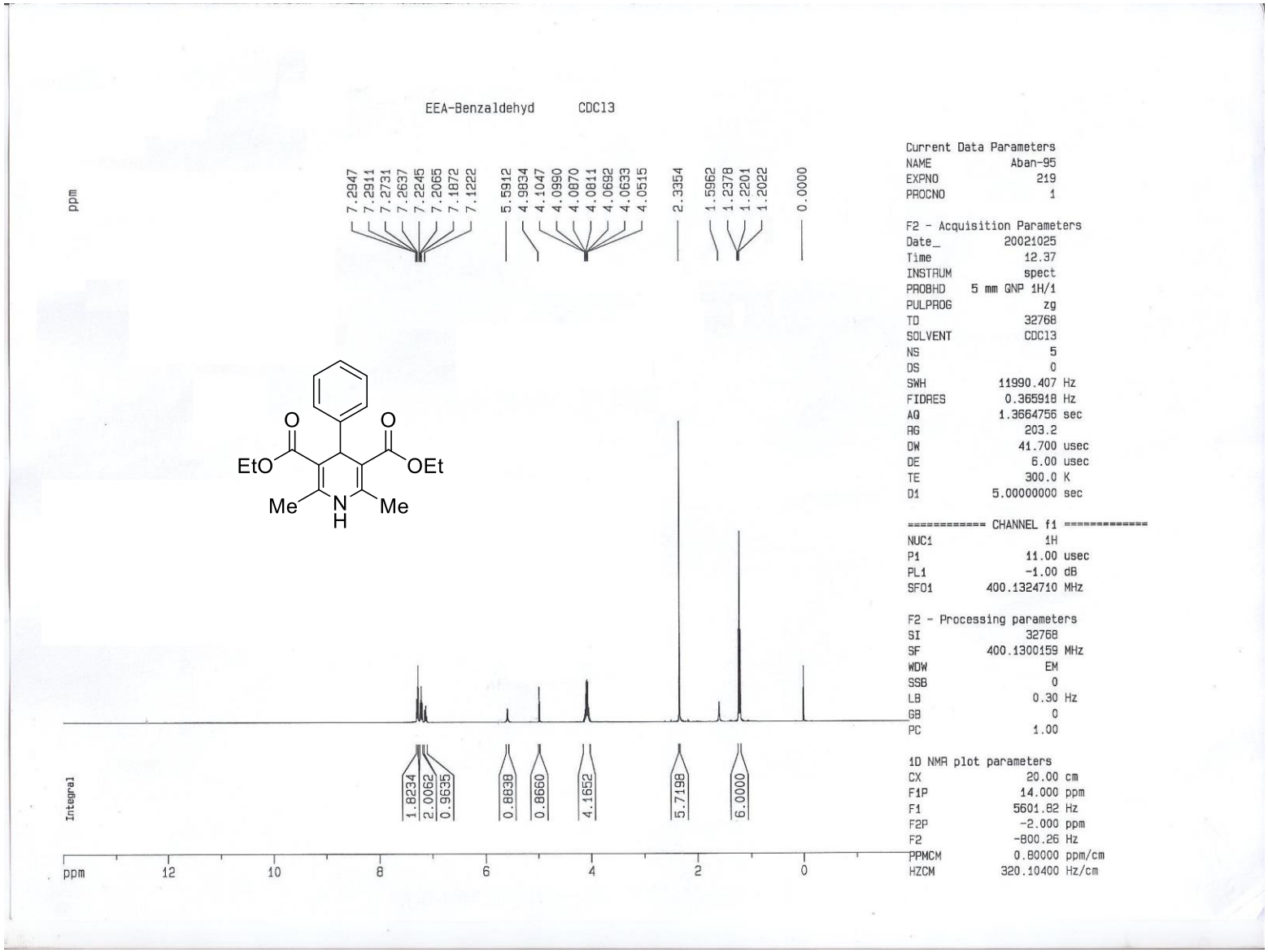

Figure S1 : ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of *diethyl 4-(4-phenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(**3a**)*

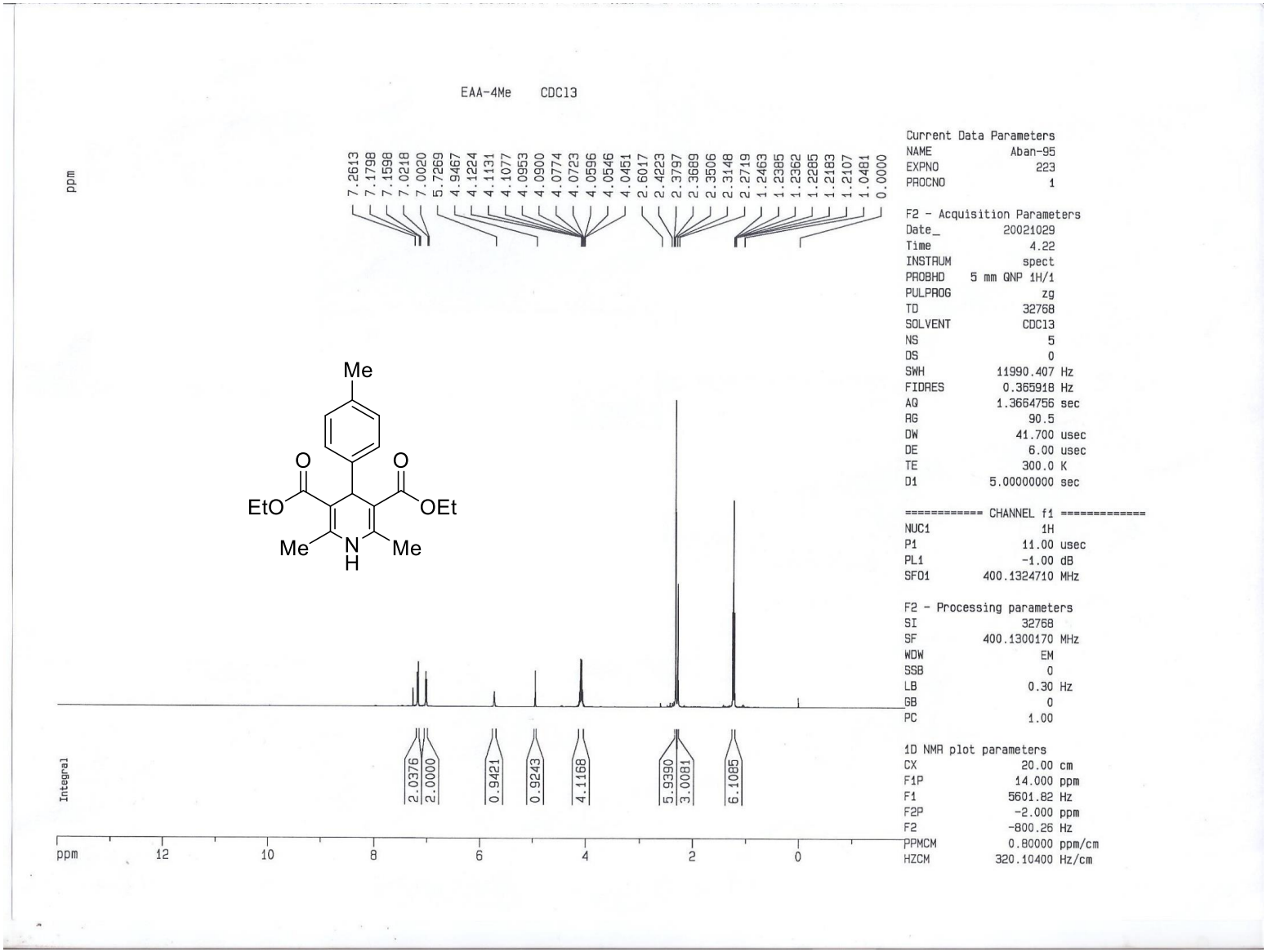

Figure S2 : ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of *diethyl 4-(4-methylphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(**3b**)*

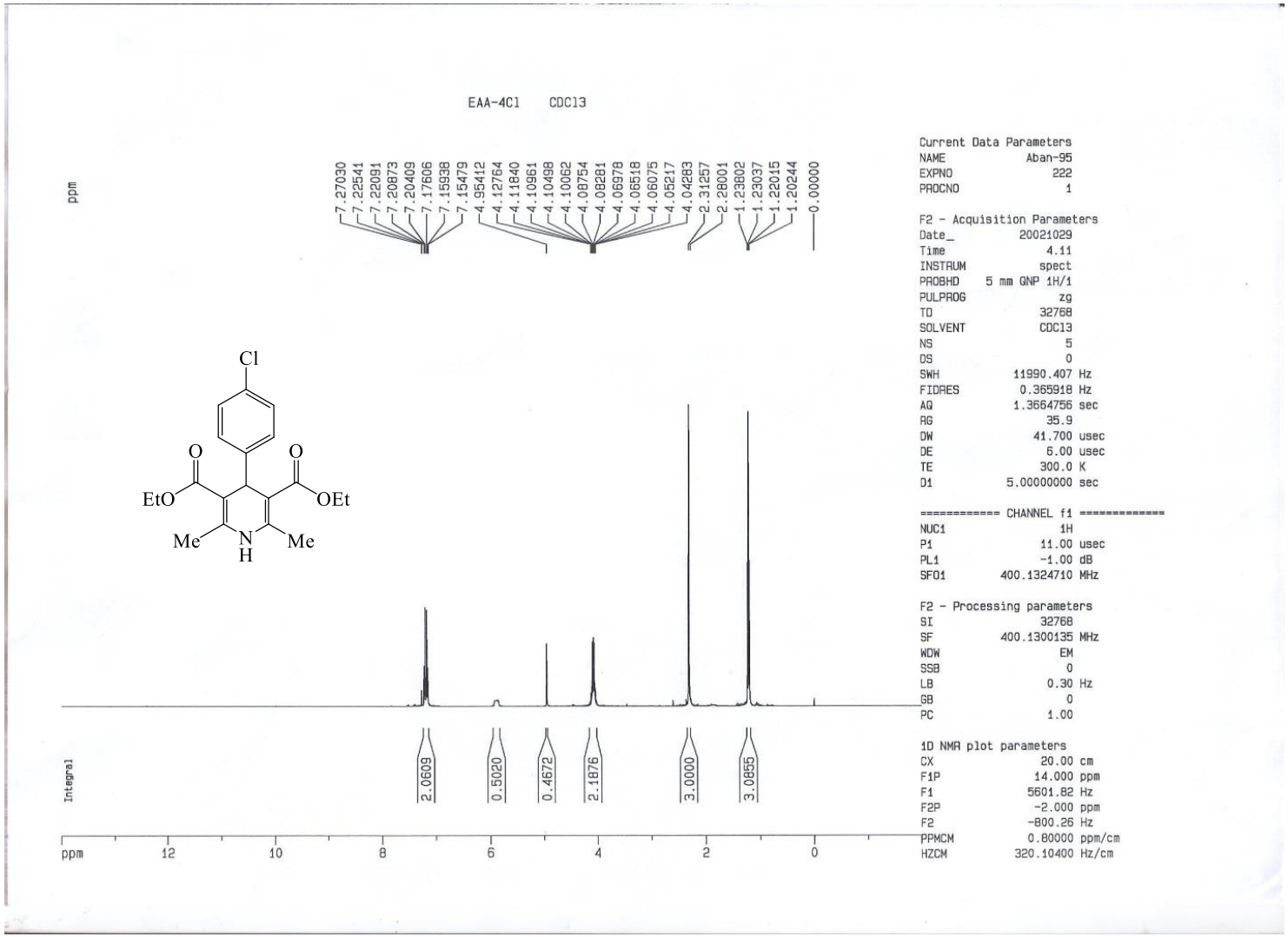

Figure S3 : ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of *diethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(**3d**)*

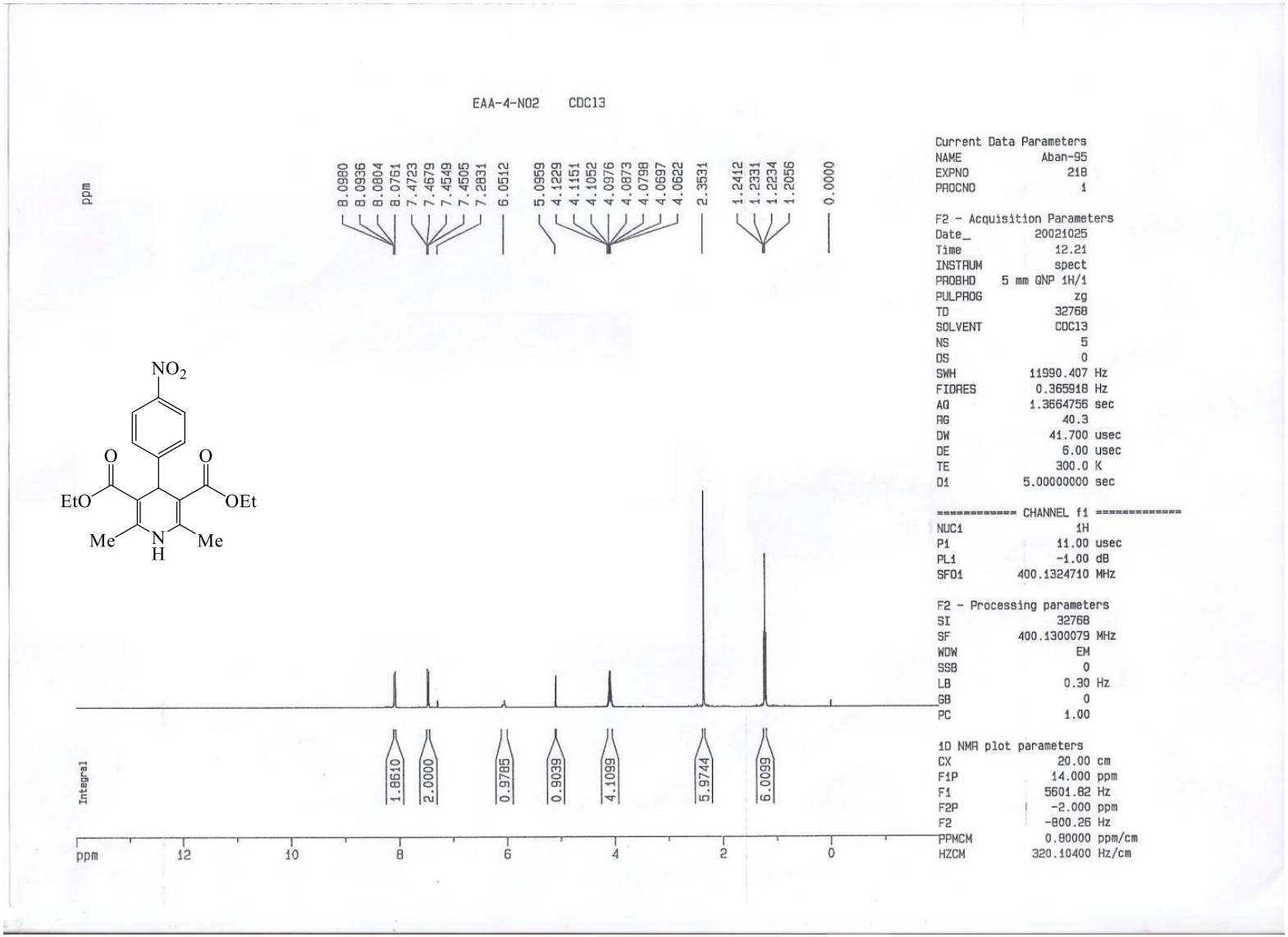

Figure S4 : ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of *diethyl 4-(4-nitrophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(**3e**)*

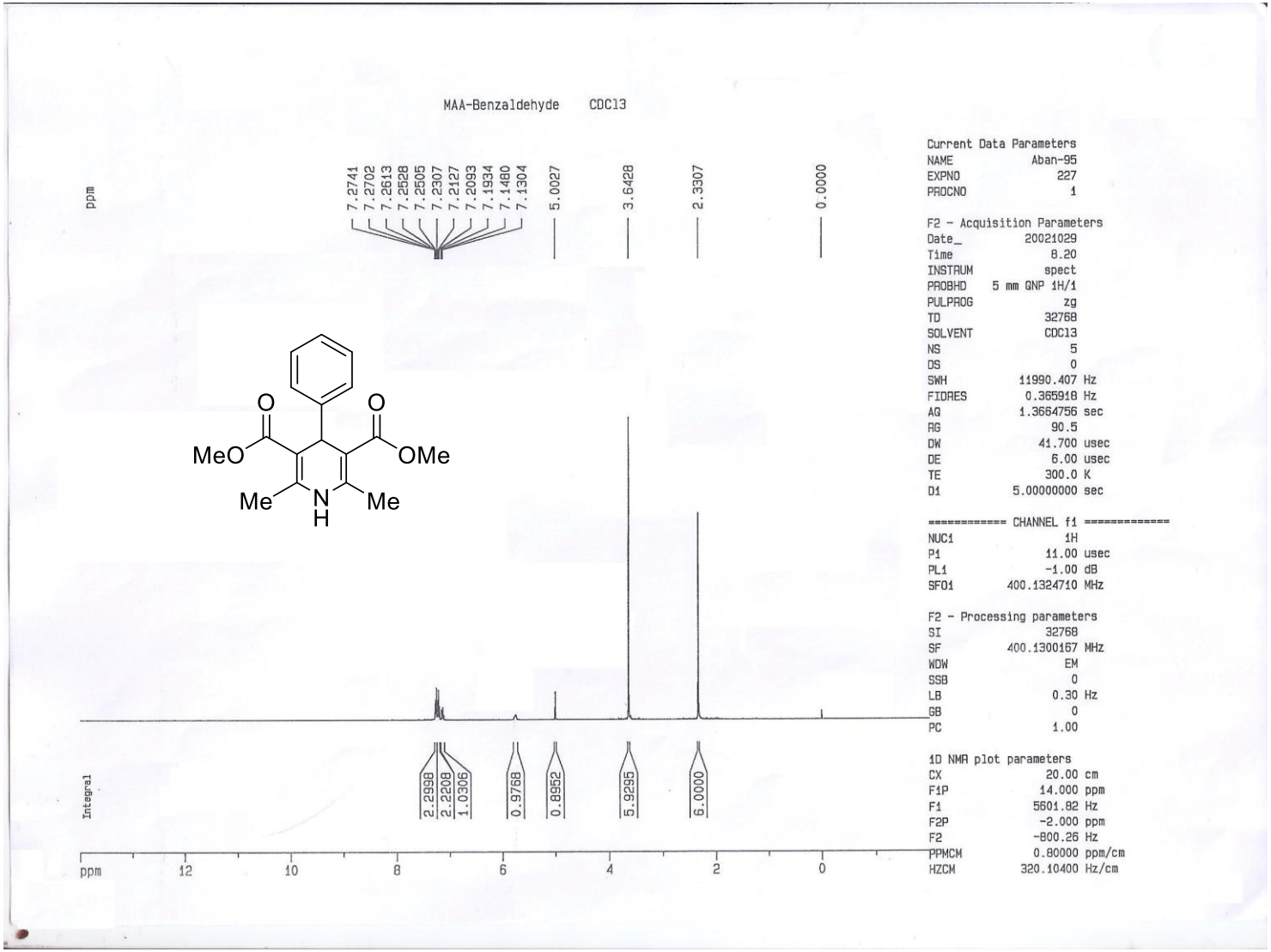

Figure S5 : ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of *dimethyl 4-(4-phenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5dicarboxylate(**3f**)*

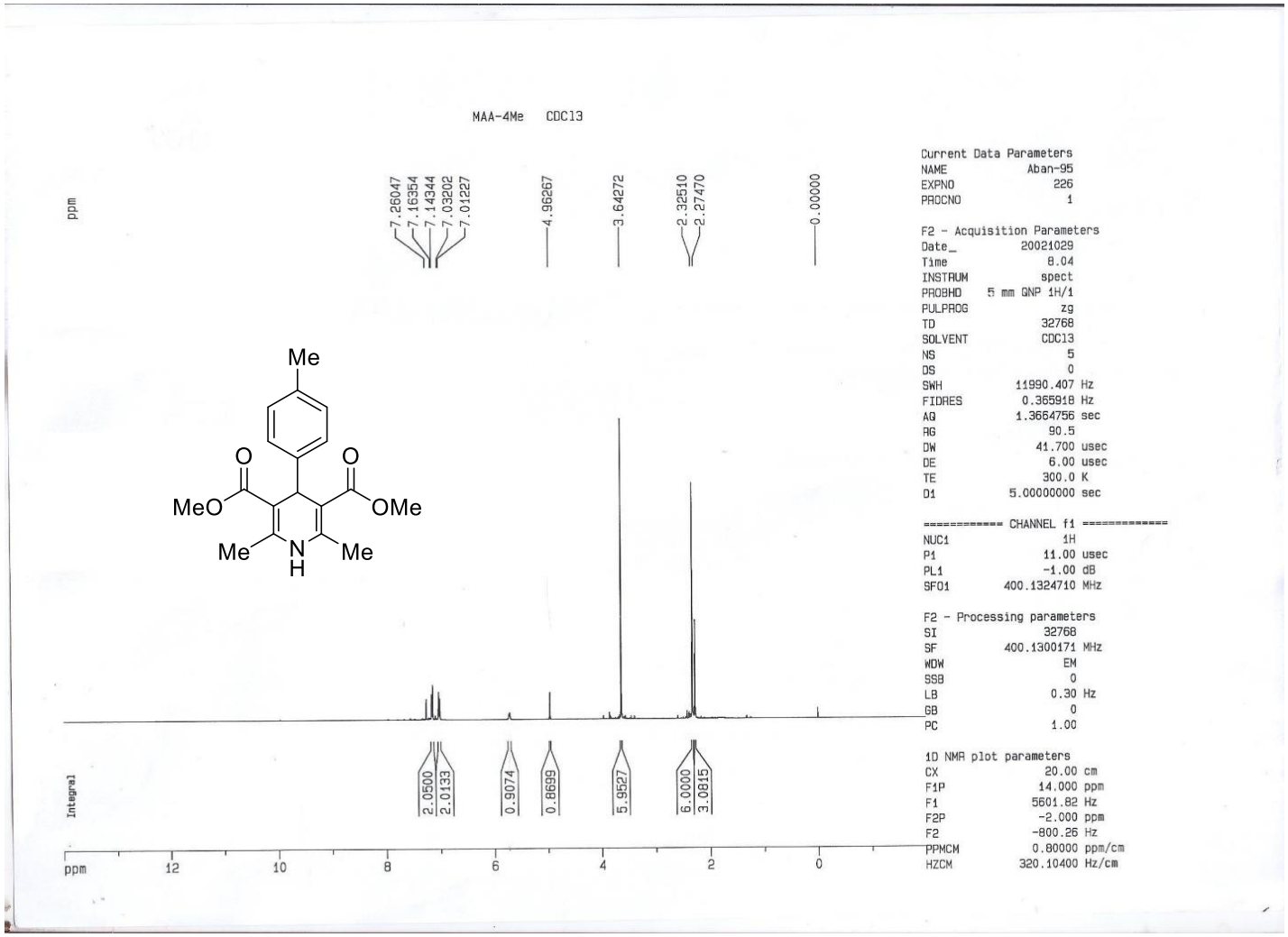

Figure S6 : ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of *dimethyl 4-(4-methylphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(**3g**)*

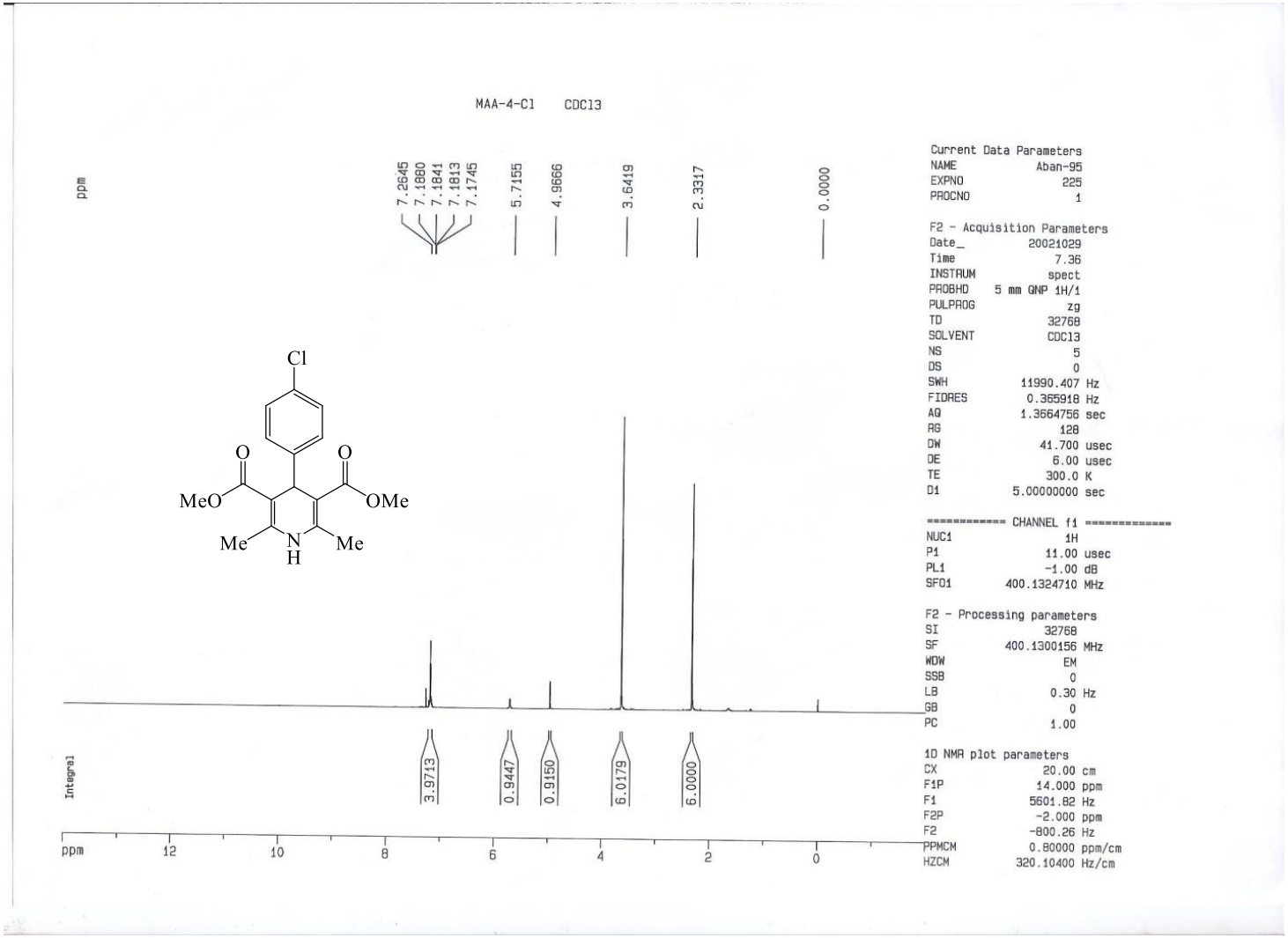

Figure S7 : ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of *dimethyl 4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(**3i**)*

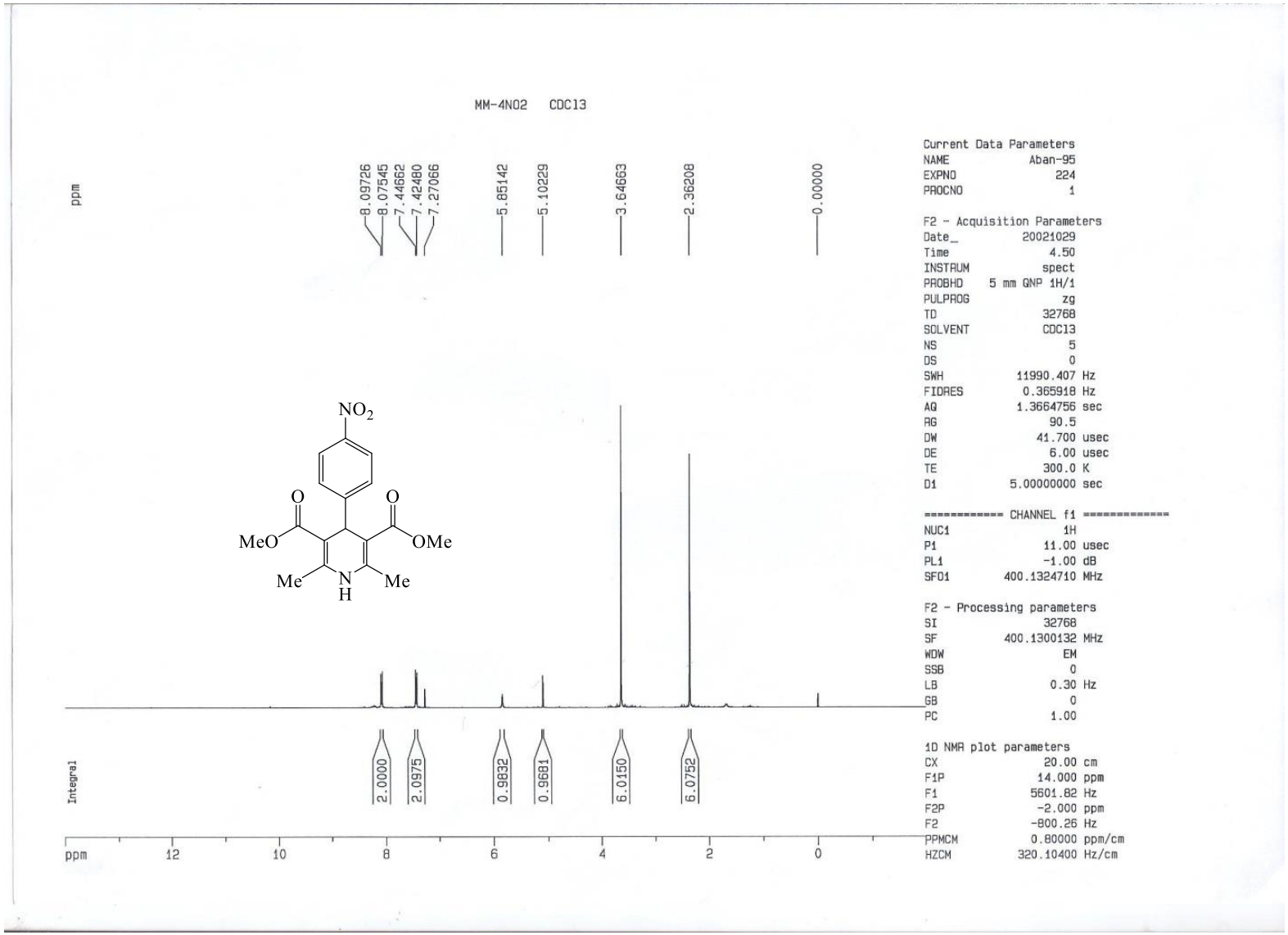

Figure S8 : ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of *dimethyl 4-(4-nitrophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate(**3j**)*