SYNTHESIS AND TRANSFORMATIONS OF ALKYL 1,5-BIS-
(DIMETHYLAMINO)-3-OXOPENTA-1,4-DIENE-2,4-DICARBOXYLATES.
A SIMPLE SYNTHESIS OF DIALKYL 1-SUBSTITUTED 4-OXO-1,4-
DIHYDROPYRIDINE-3,5-DICARBOXYLATES

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Dedicated to Professor Richard Neidlein, University of Heidelberg, on the occasion of his 70th birthday

Abstract – Dimethyl (2a) and diethyl 1,5-bis(dimethylamino)-3-oxo-penta-1,4-
diene-2,4-dicarboxylate (2b), available in good yields from the corresponding dialkyl acetonedicarboxylates (1a, b) and N,N-dimethylformamide dimethyl acetal (DMFDMA), were used as reagents for a one-step preparation of 1-
substituted 1,4-dihydropyridin-4-ones (3a–u). Thus, compounds (2) were treated with ammonia, hydrazines, and primary aliphatic, aromatic, or heterocyclic amines to form dialkyl 1-substituted 4-oxo-1,4-dihydropyridine-3,5-
dicarboxylates (3a–u).

There are several methods for the preparation of 4-oxo-1,4-dihydropyridine derivatives described in the literature.1–3 1-Substituted 4-oxo-1,4-dihydropyridinecarboxylic acid moiety is found in several drugs with antibacterial activity, such as nalidixic acid,4 oxolinic acid,5 pyridonic acid,6 and pipemidic acid.7

The outstanding activity of fluoridone as a terrestrial and aquatic herbicide8 has stimulated considerable work toward discovering alternative methods for the synthesis of 3,5-disubstituted 4(1H)-pyridinones.

1-Substituted 3,5-dinitro-4-oxo-1,4-dihydropyridines react with diethyl sodio 3-oxo-pentanedioate to give 1-substituted 3,5-bis(ethoxycarbonyl)-4-oxo-1,4-dihydropyridines.9–11 4-Oxo-1,4-dihydropyridine-3-carboxylate and its 5-substituted derivatives have been prepared by reacting of 1,3,5-triazine with 4-substituted ethyl acetoacetates in ethanol in the presence of sodium ethoxide.12,13 However, there are only few methods available for the preparation of dialkyl 4-oxo-1,4-dihydropyridine-3,5-dicarboxylates.
Diethyl acetonedicarboxylate condenses with triethyl orthoformate in hot acetic anhydride, followed by treatment of the product with ammonia to give diethyl 4-oxo-1,4-dihydropyridine-3,5-dicarboxylate in poor yield (only 4%). The intermediate, the di(ethoxyvinyl) ketone has not been isolated. 3-Chloroaniline has been used to obtain the corresponding N-(3-chlorophenyl) substituted derivative in 17% yield. Recently, the ring transformation of 3-methyl-5-nitropyrimidin-4(3H)-one, as an activated diformylamine, produces in the presence of bidentate enolate anions pyridin-4(1H)-ones functionalized at the 3- and 5-position.

Scheme 1
In the course of our studies we have prepared 2-acylamino-3-(dimethylamino)propenoates and their analogs, as masked α-formyl-α-amino- and α-formyl-α-hydroxy acids, and their derivatives. They have been applied as reagents for the preparation of a variety of heterocyclic systems with an amino or hydroxy acid structural element incorporated into the newly formed heterocyclic system. Among these systems are: pyridinones, pyrimidinones, pyranones, pyrroles, imidazoles, 1,2,4-oxadiazoles, and others.\(^{17}\)

In continuation of our research in this area, we report now a simple synthesis of dialkyl 4-oxo-1,4-dihydropyridine-3,5-dicarboxylates. In this manner, dimethyl (1a) or diethyl acetonedicarboxylate (1b) was transformed with \(N,N\)-dimethylformamide dimethyl acetal (DMFDMA) by heating in etanol for 1.5 h into dimethyl (2a) or diethyl 1,5-bis(dimethylamino)-3-oxo-penta-1,4-diene-2,4-dicarboxylate (2b) in good yield. Dialkyl 1,5-bis(dimethylamino)-3-oxo-penta-1,4-diene-2,4-dicarboxylates (2a,b) were not isolated in analytically pure form and were used without purification for further transformations. IR, \(^1\)H NMR, \(^{13}\)C NMR, and HRMS spectral data for diethyl 1,5-bis(dimethylamino)-3-oxo-penta-1,4-diene-2,4-dicarboxylate (2b) are in agreement with the proposed structure. Compounds (2) were treated with ammonia, hydrazines, primary aliphatic, aromatic, or heterocyclic amines to form dialkyl 1-substituted 4-oxo-1,4-dihydropyridine-3,5-dicarboxylates (3a–t). 1,4-Diaminobenzene reacts with 2 in 1:2 molar ratio to produce 1,4-bis[3,5-bis(methoxycarbonyl)-4-oxo-1,4-dihydropyridinyl-1]benzene (3u) in 57% yield. Reaction with hydrazine could theoretically afford either the 1-aminopyridine (3g) or the diazepine (4). Formation of the pyridone (3g) was confirmed by treatment with DMFDMA which gave the amidine (5), thus proving the 1-aminopyridine structure (Scheme 1).

**EXPERIMENTAL**

Melting points were taken on a Kofler micro hot stage. The \(^1\)H NMR spectra was obtained on a Bruker Avance DPX 300 (300 MHz) spectrometer with DMSO–d\(_6\) as solvent and Me\(_4\)Si as internal standard. The microanalyses for C, H, and N were obtained on a Perkin-Elmer CHN Analyser 2400. Mass spectra were obtained on an Autospec Q spectrometer.

**Diethyl 1,5-Bis(dimethylamino)-3-oxopenta-1,4-diene-2,4-dicarboxylate (2b).** A mixture of diethyl 1,3-acetondicarboxylate (0.95 mL, 5 mmol), \(N,N\)-dimethylformamide dimethyl acetal (95%, 2.7 ml, 19.3 mmol), and ethanol (4 mL) was refluxed for 1.5 h. Volatile components were evaporated in vacuo and the residue was purified by flash chromatography (silica gel, chloroform-methanol, 95:5). Fractions containing the product were combined and evaporated in vacuo to give 2b as a yellow oil in 50% yield. MS (FAB): m/z = 313 (MH\(^+\)). IR (film, cm\(^{-1}\)): 2981, 1682, 1594. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 1.20 (6H, t, \(J = 6.9\) Hz, \(\text{CH}_3\text{CH}_2\)); 3.02 (12H, s, NMe\(_2\)); 4.10 (4H, q, \(J = 6.9\) Hz, \(\text{CH}_2\text{CH}_3\)); 7.58 (2H, s, 1–H,
5-H). $^{13}$C NMR (75 MHz, DMSO-d$_6$): δ 14.3, 44.4, 59.4, 105.1, 155.0, 168.1, 189.2. HRMS Calcd for C$_{15}$H$_{24}$N$_2$O$_5$: 312.169400. Found: 312.168522 (M$^+$).

**General Procedure for the Preparation of Dialkyl 1-Substituted 1,4-Dihydro-4-oxopyridine-3,5-dicarboxylates (3a–t).** A mixture of dialkyl 1,3-acetonedicarboxylate (I) (5 mmol); propyl acetate (15 mL); and DMFDMA (95%, 2.7 mL, 19.3 mmol) was refluxed for 1.5 h. Volatile components were evaporated in vacuo to give a crude 2 as a brown oil which was dissolved in an alcohol (10 mL, 2a: in methanol, 2b: in ethanol). To this solution amine (7.5 mmol) was added and the mixture was refluxed for 1–28 h. The reaction mixture was concentrated to one half of the volume, cooled, and the precipitate was collected by filtration to give 3.

In this manner, the following compounds were prepared:

**Dimethyl 1,4-Dihydro-4-oxopyridine-3,5-dicarboxylate (3a).** This compound was prepared from 2a and ammonia in methanol, reflux for 2 h, yield 34%; mp 258–268° (from DMF). IR (KBr, cm$^{-1}$): 3422, 3062, 1713, 1280, 815. $^1$H NMR (300 MHz, DMSO-d$_6$): δ 3.73 (6H, s, OMe); 8.19 (2H, s, 2–H and 6–H); 11.00–12.00 (1H, br s, 1–H). $^{13}$C NMR (75 MHz, DMSO-d$_6$): δ 50.9, 120.7, 142.0, 164.4, 169.9. Anal. Calcd for C$_9$H$_9$NO$_5$: C, 51.19; H, 4.30; N, 6.63. Found: C, 51.21; H, 4.31; N, 6.54.

**Diethyl 1,4-Dihydro-4-oxopyridine-3,5-dicarboxylate (3b).** This compound was prepared from 2b and ammonia in ethanol, reflux for 2h, yield 60%; mp 238–240° (from DMF). MS (EI): m/z = 239 (M$^+$). IR (KBr, cm$^{-1}$): 3404, 3062, 1694, 1280, 815. $^1$H NMR (300 MHz, DMSO-d$_6$): δ 1.26 (6H, t, J = 6.9 Hz, CH$_3$CH$_2$); 4.21 (4H, q, J = 6.9 Hz, CH$_2$CH$_3$); 8.16 (2H, s, 2–H and 6–H); 11.00–12.00 (1H, s, 1–H). $^{13}$C NMR (75 MHz, DMSO-d$_6$): δ 13.6, 59.7, 120.8, 141.9, 164.0, 169.8. Anal. Calcd for C$_{14}$H$_{14}$NO$_5$: C, 55.23; H, 5.48; N, 5.85. Found: C, 55.30; H, 5.66; N, 5.98.

**Dimethyl 1,4-Dihydro-1-(2-propyl)-4-oxopyridine-3,5-dicarboxylate (3c).** This compound was prepared from 2a and isopropylamine in methanol, reflux for 5 h, yield 17%; mp 136–146° (from MeOH). IR (KBr, cm$^{-1}$): 3445, 2981, 1740, 1598, 1283, 818. $^1$H NMR (300 MHz, DMSO-d$_6$): δ 1.40 (6H, d, J = 6.6 Hz, Me$_2$CH); 3.73 (6H, s, Me); 4.45 (1H, m, J = 6.6, CHMe$_2$); 8.35 (2H, s, 2–H and 6–H). $^{13}$C NMR (75 MHz, DMSO-d$_6$): δ 21.7, 51.7, 58.61, 122.1, 142.6, 164.8, 170.1. Anal. Calcd for C$_{14}$H$_{14}$NO$_5$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.62; H, 6.08; N, 5.43.

**Diethyl 1,4-Dihydro-1-[(2-hydroxyethyl)amino]-4-oxopyridine-3,5-dicarboxylate (3d).** This compound was prepared from 2b and 2-hydroxyethylhydrazine in ethanol, reflux for 1.5 h, yield 21%; mp
102–105° (from n-propanol). IR (KBr, cm⁻¹): 3462, 2977, 1731, 1510, 1265, 1026, 822.¹H NMR (300 MHz, DMSO-d₅): δ 1.26 (6H, t, J = 7.2 Hz, CH₂CH₂); 3.10 (2H, m, J = 5.3 Hz, CH₂NH); 3.46 (2H, m, J = 5.13 Hz, CH₂OH); 4.20 (4H, q, J = 7.2 Hz, CH₂CH₃); 4.78 (1H, t, J = 5.1 Hz, OH); 7.03 (1H, t, J = 5.3 Hz, 1–H); 8.26 (2H, s, 2–H and 6–H).¹³C NMR (75 MHz, DMSO-d₆): δ 14.1, 54.0, 54.1, 58.1, 58.2, 60.4, 121.3, 145.86, 145.89, 163.7, 169.8. Anal. Calcd for C₁₃H₁₈N₂O₆: C, 52.35; H, 6.08; N, 9.39. Found: C, 52.38; H, 6.03; N, 9.31.

Diethyl 1,4-Dihydro-1-(1-hydroxybutyl-2)-4-oxopyridine-3,5-dicarboxylate (3e). This compound was prepared from 2b and 2-amino-1-butanol in ethanol, reflux for 20 h, yield 28%; mp 124–130° (from EtOH). IR (KBr, cm⁻¹): 3367, 2982, 1738, 1689, 1523, 1273, 1172, 810.¹H NMR (300 MHz, DMSO-d₆): δ 0.83 (3H, t, J = 7.5 Hz, CH₃CH₂CH₂); 1.26 (6H, t, J = 7.2 Hz, OCH₂CH₂); 1.74 (2H, q, J = 7.5 Hz CH₂CH₂CH₃); 3.65 (2H, t, J = 7.0 Hz, CH₂OH); 4.08 (1H, m, CHCH₂CH₃); 4.20 (4H, q, J = 7.2 Hz, OCH₂CH₃); 5.15 (1H, t, J = 7.0 Hz, OH); 8.25 (2H, s, 2–H and 6–H).¹³C NMR (75 MHz, DMSO-d₆): δ 10.0, 14.1, 22.6, 60.4, 62.2, 70.1, 122.1, 143.4, 164.4, 170.5. Anal. Calcd for C₁₃H₂₁NO₆: C, 57.87; H, 6.80; N, 4.50. Found: C, 57.51; H, 6.80; N, 4.65.

Diethyl 1,4-Dihydro-1-(ethoxycarbonylmethyl)-4-oxopyridine-3,5-dicarboxylate (3f). This compound was prepared from 2b and ethyl glycinate hydrochloride in ethanol, reflux for 21 h, yield 33%; mp 175–177° (from EtOH). IR (KBr, cm⁻¹): 2995, 1738, 1481, 1171.¹H NMR (300 MHz, DMSO-d₆): δ 1.21–1.28 (9H, m, OCH₂CH₂); 4.10–4.25 (6H, m, OCH₂CH₃); 4.98 (2H, s, CH₂COEt); 8.31 (2H, s, 2–H and 6–H).¹³C NMR (75 MHz, DMSO-d₆): δ 14.0, 14.1, 56.1, 60.4, 61.5, 121.6, 146.2, 163.9, 168.1, 170.1. Anal. Calcd for C₁₃H₁₉NO₂: C, 55.38; H, 5.89; N, 4.31. Found: C, 54.99; H, 5.69; N, 4.21.

Diethyl 1-Amino-1,4-dihydro-4-oxopyridine-3,5-dicarboxylate (3g). This compound was prepared from 2b and hydrazine hydrate in ethanol, reflux for 3 h, yield 34%; mp 127–130° (from EtOH). MS (El): m/z = 254 (M⁺). IR (KBr, cm⁻¹): 3466, 3283, 3176, 2980, 1731,1570, 1262.¹H NMR (300 MHz, DMSO-d₆): δ 1.25 (6H, t, J = 6.9 Hz, CH₂CH₃); 4.19 (4H, q, J = 6.9 Hz, CH₂CH₃); 6.66 (2H, s, NH₂); 8.14 (2H, s, 2–H and 6–H).¹³C NMR (75 MHz, DMSO-d₆): δ 14.1, 60.3, 120.7, 146.5, 163.6, 169.6. Anal. Calcd for C₁₁H₁₄N₂O₂: C, 51.97; H, 5.55; N, 11.02. Found: C, 51.85; H, 5.66; N, 11.13.

Diethyl 1,4-Dihydro-1-phenyl-4-oxopyridine-3,5-dicarboxylate (3h). This compound was prepared from 2b and aniline in ethanol, reflux for 28 h, yield 62%; mp 151–154° (from EtOH). MS (El): m/z = 315 (M⁺). IR (KBr, cm⁻¹): 2985, 1745, 1264, 712.¹H NMR (300 MHz, DMSO-d₆): δ 1.26 (6H, t, J = 6.9 Hz, CH₂CH₃); 4.21 (4H, q, J = 6.9, CH₂CH₃); 7.45–7.70 (5H, m, Ph); 8.41 (2H, s, 2–H and 6–H).¹³C
NMR (75 MHz, DMSO-d$_6$): $\delta$ 14.1, 60.5, 122.4, 123.5, 128.9, 129.9, 142.2, 143.5, 163.8, 170.1. Anal. Calcd for C$_{17}$H$_{17}$NO$_5$: C, 64.75; H, 5.43; N, 4.44. Found: C, 65.14; H, 5.42; N, 4.36.

**Diethyl 1,4-Dihydro-1-(4-methylphenyl)-4-oxopyridine-3,5-dicarboxylate (3i).** This compound was prepared from 2b and 4-methylaniline in ethanol, reflux for 2 h, yield 92%; mp 137–141$^\circ$ (from EtOH). IR (KBr, cm$^{-1}$): 1796, 1740, 1694, 1267. $^1$H NMR (300 MHz, DMSO-d$_6$): $\delta$ 1.26 (6H, t, $J = 7.2$ Hz, CH$_2$CH$_3$); 2.38 (3H, s, ArCH$_3$); 4.21 (4H, q, $J = 7.2$ Hz, CH$_2$CH$_3$); 7.37 (2H, dd, $J = 2.1$, 8.7 Hz, 2H–Ar); 7.55 (2H, dd, $J = 2.1$, 8.7 Hz, 2H–Ar); 8.36 (2H, s, 2–H and 6–H). $^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta$ 14.1, 20.5, 60.5, 122.4, 123.3, 130.3, 138.6, 139.9, 143.5, 163.8, 170.0. Anal. Calcd for C$_{15}$H$_{19}$NO$_5$: C, 65.64; H, 5.81; N, 4.25. Found: C, 65.40; H, 5.76; N, 4.56.

**Diethyl 1,4-Dihydro-1-[4-(hydroxymethyl)phenyl]-4-oxopyridine-3,5-dicarboxylate (3j).** This compound was prepared from 2b and 4-(hydroxymethyl)aniline in ethanol, reflux for 2.5 h, yield 86%; mp 226–230$^\circ$ (from EtOH). IR (KBr, cm$^{-1}$): 3393, 2984, 1737, 1267, 1027. $^1$H NMR (300 MHz, DMSO-d$_6$): $\delta$ 1.24 (6H, t, $J = 7.2$ Hz, CH$_2$CH$_3$); 4.19 (4H, q, $J = 7.2$ Hz, CH$_2$CH$_3$); 4.41 (2H, d, $J = 5.1$ Hz, CH$_2$OH); 5.37 (1H, d, $J = 5.1$ Hz, OH); 7.56 (4H, m, Ph); 8.25 (2H, s, 2–H and 6–H). $^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta$ 14.1, 59.2, 60.4, 121.7, 126.7, 128.7, 129.7, 130.0, 137.3, 140.7, 145.1, 163.7, 170.1. Anal. Calcd for C$_{18}$H$_{19}$NO$_6$: C, 62.60; H, 5.55; N, 4.06. Found: C, 62.84; H, 5.50; N, 4.12.

**Diethyl 1,4-Dihydro-1-(2-aminophenyl)-4-oxopyridine-3,5-dicarboxylate (3k).** This compound was prepared from 2b and 2-aminoaniline in ethanol, reflux for 20 h, yield 77%; mp 127–130$^\circ$ (from EtOH). IR (KBr, cm$^{-1}$): 3438, 3323, 3223, 1746, 1651, 1265, 1031. $^1$H NMR (300 MHz, DMSO-d$_6$): $\delta$ 1.24 (6H, t, $J = 7.2$ Hz, CH$_2$CH$_3$); 4.19 (4H, q, $J = 7.2$ Hz, CH$_2$CH$_3$); 5.49 (2H, s, NH$_2$); 6.66 (1H, deg dt, $J = 7.9$, 1.5 Hz, 1H–Ar); 6.86 (1H, dd, $J = 8.2$, 1.2 Hz, 1H–Ar); 7.22 (2H, m, 2H–Ar); 8.05 (2H, s, 2–H and 6–H). $^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta$ 14.1, 60.3, 116.4, 116.6, 122.3, 127.1, 127.4, 130.4, 143.3, 145.6, 163.7, 170.5. Anal. Calcd for C$_{17}$H$_{15}$N$_2$O$_5$: C, 61.81; H, 5.49; N, 8.48. Found: C, 61.92; H, 5.40; N, 8.42.

**Dimethyl 1,4-Dihydro-1-(4-hydroxyphenyl)-4-oxopyridine-3,5-dicarboxylate (3l).** This compound was prepared from 2a and 4-hydroxyaniline in methanol, reflux for 2 h, yield 76%; mp 262–270$^\circ$ (from DMF). IR (KBr, cm$^{-1}$): 3455, 3062, 1742, 1704, 1515, 1279, 1237. $^1$H NMR (300 MHz, DMSO-d$_6$): $\delta$ 3.74 (6H, s, OMe); 6.90 (2H, dd, $J = 6.6$, 2.4 Hz, 2H–Ph); 7.46 (2H, dd, $J = 6.6$, 2.4 Hz, 2H–Ph); 8.32 (2H, s, 2–H and 6–H); 10.00 (1H, s, OH). $^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta$ 51.8, 116.1, 121.9, 125.0, 134.1, 144.3, 157.9, 164.3, 169.9. Anal. Calcd for C$_{15}$H$_{13}$NO$_6$: C, 59.41; H, 4.32; N, 4.62. Found: C, 59.62; H, 4.37; N, 4.52.
Dimethyl 1,4-Dihydro-1-(3-bromophenyl)-4-oxopyridine-3,5-dicarboxylate (3m). This compound was prepared from 2a and 3-bromoaniline in methanol, reflux for 1 h; yield 75%; mp 274–276° (from MeOH). IR (KBr, cm⁻¹): 3059, 1752, 1643, 1277, 1145, 814. ¹H NMR (300 MHz, DMSO-d₆): δ 3.75 (6H, s, OMe); 7.53 (1H, deg t, J = 8.1 Hz, 1H–Ar); 7.71 (2H, m, 2H–Ar); 8.01 (1H, deg t, J = 1.8 Hz, 1H–Ar); 8.46 (2H, s, 2–H and 6–H). ¹³C NMR (75 MHz, DMSO-d₆): δ 51.7, 121.97, 122.02, 122.6, 126.4, 131.5, 131.6, 143.1, 143.6, 164.0, 169.9. Anal. Calcd for C₁₃H₁₂NO₃Br: C, 49.20; H, 3.30; N, 3.83. Found: C, 49.22; H, 3.28; N, 3.61.

Diethyl 1,4-Dihydro-1-(3,4-methylenedioxyphenyl)-4-oxopyridine-3,5-dicarboxylate (3n). This compound was prepared from 2b and 3,4-methylenedioxyaniline in ethanol, reflux for 3 h; yield 94%; mp 194–196° (from EtOH). IR (KBr, cm⁻¹): 2986, 1739, 1694, 1263, 1067. ¹H NMR (300 MHz, DMSO-d₆): δ 1.26 (6H, t, J = 7.2 Hz, CH₂CH₃); 4.21 (4H, q, J = 7.2 Hz, CH₂CH₃); 6.15 (2H, s, CH₂); 7.07 (1H, t, J = 7.7 Hz, 1H–Ar); 7.13 (1H, dd, J = 7.7, 2.4 Hz, 1H–Ar); 7.37 (1H, d, J = 2.4 Hz, 1H–Ar); 8.30 (2H, s, 2–H and 6–H). ¹³C NMR (75 MHz, DMSO-d₆): δ 14.1, 60.5, 102.3, 105.5, 108.4, 117.6, 122.1, 136.6, 144.0, 147.6, 148.0, 163.8, 170.0. Anal. Calcd for C₁₈H₁₇NO₇: C, 60.17; H, 4.77; N, 3.90. Found: C, 60.38; H, 4.67; N, 3.64.

Diethyl 1,4-Dihydro-1-(5-methylisoxazolyl-3)-4-oxopyridine-3,5-dicarboxylate (3o). This compound was prepared from 2b and 3-amino-5-methylisoxazole in ethanol, reflux for 19 h; yield 63%; mp 145–148° (from EtOH). IR (KBr, cm⁻¹): 3131, 1736, 1695, 1471, 1270, 814. ¹H NMR (300 MHz, DMSO-d₆): δ 1.28 (6H, t, J = 7.2 Hz, CH₂CH₃); 2.50 (3H, s, 5’–CH₃); 4.25 (4H, q, J = 7.2 Hz, CH₂CH₃); 7.07 (1H, s, 4’–H); 8.60 (2H, s, 2–H and 6–H). ¹³C NMR (75 MHz, DMSO-d₆): δ 12.5, 14.1, 60.9, 95.4, 122.7, 140.1, 160.4, 163.3, 170.6, 173.4. Anal. Calcd for C₁₅H₁₆N₂O₆: C, 56.25; H, 5.03; N, 8.75. Found: C, 56.11; H, 4.88; N, 8.76.

Diethyl 1,4-Dihydro-1-(thiazolyl-2)-4-oxopyridine-3,5-dicarboxylate (3p). This compound was prepared from 2b and 2-aminothiazole in ethanol, reflux for 21 h; yield 34%; mp 170–173° (from EtOH). IR (KBr, cm⁻¹): 3079, 1734, 1639, 1261, 1030. ¹H NMR (300 MHz, DMSO-d₆): δ 1.28 (6H, t, J = 7.2 Hz, CH₂CH₃); 4.25 (4H, q, J = 7.2 Hz, CH₂CH₃); 7.75 (1H, d, J = 1.5 Hz, 1H–thiazole); 7.78 (1H, d, J = 1.5 Hz, 1H–thiazole); 8.75 (2H, s, 2–H and 6–H). ¹³C NMR (75 MHz, DMSO-d₆): δ 14.1, 60.9, 120.2, 122.3, 140.2, 140.4, 160.8, 163.3, 170.6. Anal. Calcd for C₁₄H₁₄N₂O₃S: C, 52.17; H, 4.38; N, 8.69. Found: C, 52.00; H, 4.33; N, 8.37.

Diethyl 1,4-Dihydro-1-(pyridinyl-2)-4-oxopyridine-3,5-dicarboxylate (3q). This compound was prepared from 2b and 2-aminopyridine in ethanol, reflux for 17 h; yield 66%; mp 149–151° (from EtOH).
IR (KBr, cm⁻¹): 3391, 2978, 1709, 1659, 1244. ¹H NMR (300 MHz, DMSO-d₆): δ 1.29 (6H, t, J = 7.2 Hz, CH₂CH₃); 4.26 (4H, q, J = 7.2 Hz, CH₂CH₃); 7.55 (1H, ddd, J=7.3, 4.9 1.0 Hz, 5'-H); 7.96 (1H, deg dt, J = 8.4, 1.0 Hz, 3'-H); 8.12 (1H, ddd, J = 8.4, 7.3, 2.0 Hz, 4'-H); 8.62 (1H, ddd, J = 4.9, 2.0, 1.0 Hz, 6'-H); 8.93 (2H, s, 2-H and 6-H). ¹³C NMR (75 MHz, DMSO-d₆): δ 14.1, 60.7, 114.6, 122.2, 123.7, 140.3, 140.4, 148.7, 150.8, 163.8, 170.7. Anal. Calcd for C₁₆H₁₆N₂O₅: C, 60.75; H, 5.10; N, 8.86. Found: C, 60.88; H, 5.05; N, 8.94.

Diethyl 1,4-Dihydro-1-(6-methylpyridinyl-2)-4-oxopyridine-3,5-dicarboxylate (3r). This compound was prepared from 2b and 2-amino-6-methylpyridine in ethanol, reflux for 21 h, yield 73%; mp 170–171° (from EtOH). IR (KBr, cm⁻¹): 2985, 1745, 1450, 1271. ¹H NMR (300 MHz, DMSO-d₆): δ 1.29 (6H, t, J = 7.2 Hz, CH₂CH₃); 2.56 (3H, s, 6'-Me); 4.25 (4H, q, J = 7.2 Hz, CH₂CH₃); 7.40 (1H, d, J = 8.4 Hz, 5'-H); 7.73 (1H, d, J = 7.5 Hz, 3'-H); 7.98 (1H, dd, J = 8.4, 7.5 Hz, 4'-H); 8.90 (2H, s, 2-H and 6-H). ¹³C NMR (75 MHz, DMSO-d₆): δ 14.1, 23.7, 60.7, 111.4, 122.3, 123.0, 140.3, 140.5, 150.2, 157.9, 163.9, 170.7. Anal. Calcd for C₁₇H₁₈N₂O₅: C, 61.81; H, 5.49; N, 8.48. Found: C, 61.67; H, 5.53; N, 8.42.

Diethyl 1,4-Dihydro-1-(6-aminopyridinyl-2)-4-oxopyridine-3,5-dicarboxylate (3s). This compound was prepared from 2b and 2,6-diaminopyridine in ethanol, reflux for 3 h, yield 53%; mp 213–216° (from EtOH). IR (KBr, cm⁻¹): 3431, 3321, 3217, 1732, 1265. ¹H NMR (300 MHz, DMSO-d₆): δ 1.28 (6H, t, J = 6.9 Hz, CH₂CH₃); 4.24 (4H, q, J = 6.9 Hz, CH₂CH₃); 6.51 (1H, d, J = 8.1 Hz, 5'-H); 6.61 (2H, s, NH₂); 6.90 (1H, d, J = 7.5 Hz, 3'-H); 7.61 (1H, dd, J = 8.1, 7.5 Hz, 4'-H); 8.81 (2H, s, 2-H and 6-H). ¹³C NMR (75 MHz, DMSO-d₆): δ 14.1, 60.6, 100.1, 107.7, 122.0, 140.3, 140.3, 149.6, 159.3, 164.0, 170.7. HRMS Calcd for C₁₆H₁₇N₃O₅: 331.116821. Found: 331.117500 (M⁺).

Diethyl 1,4-Dihydro-1-(pyrimidinyl-2)-4-oxopyridine-3,5-dicarboxylate (3t). This compound was prepared from 2b and 2-aminopyrimidine in ethanol, reflux for 24 h, yield 28%; mp 158–177° (from EtOH). IR (KBr, cm⁻¹): 3088, 1734, 1698, 1345. ¹H NMR (300 MHz, DMSO-d₆): δ 1.29 (6H, t, J = 7.2 Hz, CH₂CH₃); 4.27 (4H, q, J = 7.2 Hz, CH₂CH₃); 7.64 (1H, t, J = 4.8 Hz, 5'-H); 9.00 (2H, d, J = 4.8 Hz, 4'-H and 6'-H); 9.35 (2H, s, 2-H and 6-H). ¹³C NMR (75 MHz, DMSO-d₆): δ 14.1, 60.8, 120.4, 121.6, 138.8, 154.2, 159.6, 163.5, 171.2. Anal. Calcd for C₁₅H₁₅N₃O₅: C, 56.78; H, 4.76; N, 13.24. Found: C, 56.59; H, 4.68; N, 13.60.

1,4-Bis[3,5-bis(methoxycarbonyl)-1,4-dihydro-4-oxopyridinyl-1]benzene (3u). A mixture of dimethyl 1,3-acetonedicarboxylate (1) (0.870 g, 5 mmol), propyl acetate (15 mL), and DMFDMA (95%, 2.7 mL,
19.3 mmol) was refluxed for 1.5 h. Volatile components were evaporated *in vacuo* to give a crude 2 as a brown oil which was dissolved in methanol (10 mL). To this solution 4-aminoaniline (0.270 g, 2.5 mmol) was added and the mixture was refluxed for 2.5 h. The reaction mixture was concentrated to one half of the volume, cooled, and the precipitate was collected by filtration to give 3u. Yield 57% (0.706 g); mp >350° (from AcOH). MS (EI): m/z = 496 (M⁺). IR (KBr, cm⁻¹): 3036, 1753, 1639, 1266, 1152, 816. \(^1\)H NMR (300 MHz, DMSO-d₆): δ 3.77 (12H, s, OMe); 7.86 (4H, s, 4H-Ar); 8.39 (4H, s, 2'-H and 6'-H). \(^1\)C NMR (75 MHz, CF₃COOH): δ 56.6, 119.3, 129.4, 146.2, 152.1, 166.3, 175.6. *Anal.* Calcd for C₂₄H₂₄N₂O₁₀: C, 58.07; H, 4.06; N, 5.64. Found: C, 57.87; H, 4.08; N, 5.59.

**Diethyl 1,4-Dihydro-1-[(dimethylamino)methylideneimino]-4-oxopyridine-3,5-dicarboxylate (5).** A mixture of diethyl 1- amino-1,4-dihydro-4-oxopyridine-3,5-dicarboxylate (3g) (0.912 g, 3.6 mmol); ethanol (15 mL); and DMFDMA (95%, 1 mL, 7.1 mmol) was refluxed for 2.5 h. The reaction mixture was concentrated to one half of the volume, cooled (0°C), and the precipitate was collected by filtration to give 5. Yield 71% (0.792 g); mp 137–147° (from ethanol). MS (EI): m/z = 309 (M⁺). IR (KBr, cm⁻¹): 3445, 2986, 1731, 1592, 1258. \(^1\)H NMR (300 MHz, DMSO-d₆): δ 1.25 (6H, t, J = 7.2 Hz, CH₃CH₂); 2.85 (6H, s, NMe₂); 4.18 (4H, q, J = 7.2 Hz, CH₂CH₃); 8.14 (2H, s, 2'-H and 6'-H); 8.22 (1H, s, CHNMe₂). \(^1\)C NMR (75 MHz, DMSO-d₆): δ 14.1, 34.4, 60.3, 121.1, 142.4, 161.6, 163.9, 169.4. *Anal.* Calcd for C₁₄H₁₉N₃O₅: C, 54.36; H, 6.19; N, 13.58. Found: C, 54.42; H, 6.32; N, 13.94.

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**REFERENCES AND NOTES**


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