Scope and Limitations of an Efficient Four Component Reaction for Dihydropyridin-2-ones

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General Information

All reactions were carried out under an inert atmosphere of dry argon. Standard syringe techniques were applied for transfer of air sensitive reagents and dry solvents. Melting points are uncorrected. Infrared (IR) spectra are measured in KBr and wavelengths (ν) are reported in cm^{-1}. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded at 250.13 or 400.13 MHz and 62.90 or 100.62 MHz respectively with chemical shifts (δ) reported in ppm downfield from tetramethylsilane. Peak assignment was also done with the aid of *gs*-COSY, *gs*-HMQC and *gs*-HMBC measurements. Assignment of relative stereochemistry was achieved using gs-NOESY measurements. Electron Impact (EI) mass spectrometry was carried out with an electron ionization voltage of 70eV. MS (ESI) spectra were recorded on a liquid chromatograph mass spectrometer. Chromatographic purification refers to flash chromatography using the indicated solvent (mixture) and silica gel (40-63 μm, 60 Å). Thin Layer Chromatography was performed using silica plates (silica on aluminium with fluorescence indicator). Compounds on TLC were visualised by UV-detection. THF was dried and distilled from sodium benzophenone ketyl prior to use. Benzonitrile was dried with $MgSO_4$ and then distilled from P_2O_5 under reduced pressure. Isobutyronitrile and 2-furaldehyde were both distilled prior to use. Other commercially available reagents were used as purchased. Experimental details of compounds **12a**-**12n** have been reported elsewhere.[1]

Experimental part

General Procedure I for the synthesis of 3,4-dihydropyridin-2-ones: All reactions were carried out at a concentration of 0.2 M of phosphonate **1**, 0.24 M of *n*BuLi, 0.22 M of nitrile **2**, 0.22 M of aldehyde **3** and 0.22 M of isocyanoacetate **11** (or malonate / cyanoacetate **34**) in dry THF. Always 1.0 mmol of the limiting reaction component, the phosphonate, was used. 1.2 equiv. of *n*BuLi (1.6 M solution in hexane) were added at –78 °C to a stirred solution of phosphonate in THF. After stirring at –78 °C for 1.5 h the nitrile (1.1 equiv.) was added and the mixture was then stirred at –78 °C for 45 min., at –40 °C for 1 h and at –5 °C for 30 min. The aldehyde (1.1 equiv.) was added and, after stirring at –5 °C for 30 min., the mixture was allowed to warm to rt and stirred for 1.5 h. Finally the isocyanoacetate (or malonate / cyanoacetate) (1.1 equiv.) was added and the mixture was stirred overnight either at rt or at reflux. The reaction mixture was concentrated *in vacuo* (water-bath at rt) and the crude product purified by column chromatography.[2]

3,4-Dihydropyridin-2-one 12p: According to General procedure I, reaction between phosphonate **1b**, *n*BuLi, 2-furonitrile **2c**, benzaldehyde **3b** and isocyanoacetate **11a**, followed by column chromatography (*c*-hexane/EtOAc = 9:1→8:2) afforded **12p** as a yellow solid (90 mg, 0.25 mmol, 25%, *cis*). MP 218-220 ºC (decomposes); ^{1}H NMR (250 MHz, DMSO): δ= 10.23 (s, 1H), 7.69-7.65 (m, 2H), 7.49-7.37 (m, 9H), 6.71 (d, *J* = 3.5 Hz, 1H), 6.54 (m, 1H), 4.35 (s, 1H), 1.82 ppm (s, 3H); ^{13}C NMR (101 MHz, DMSO): δ= 163.1 (C), 159.9 (C), 146.5 (C), 143.1 (CH), 136.4 (C), 135.4 (C), 129.4 (CH), 129.2 (2 CH), 129.0 (2 CH), 128.6 (2 CH), 128.1 (CH), 125.6 (2 CH), 123.0 (C), 113.3 (C), 111.2

(CH), 110.3 (CH), 69.6 (C), 54.7 (CH), 17.7 ppm (CH_3); IR(KBr): 2145 (w), 1693 (s), 1495 (w), 1447 (w), 1399 (w), 1387 (w), 1298 (w), 1154 (w), 1030 (w), 748 (s), 698 (s); HRMS (EI, 70 eV): calculated for $C_{23}H_{18}N_2O_2$ (M^+) 354.1363, found 354.1351.

3,4-Dihydropyridin-2-one 12r: According to General procedure I, reaction between phosphonate **1a**, *n*BuLi, benzonitrile **2a**, benzaldehyde **3b** and isocyanoacetate **11d**, followed by column chromatography (*c*-hexane/EtOAc = 9:1→8:2) afforded **12r** at rt as a white solid (91 mg, 0.30 mmol, 30%, *cis*:*trans* = 63:37) and at reflux as a white solid (125 mg, 0.41 mnol, 41%, *cis*:*trans* = 71:29). The diastereomers could be separated using a second chromatographic purification (*c*hexane: EtOAc = 9:1, both white solids). *cis*-12r: MP 161-165 ºC (decomposes); ^{1}H NMR (250 MHz, $CDCl_3$): δ= 7.51-7.26 (m, 11H), 5.63 (dd, *J* = 1.5, 6.3 Hz, 1H), 3.81 (d, *J* = 6.3 Hz, 1H), 2.34-2.20 (m, 1H), 2.13-2.00 (m, 1H), 1.21 ppm (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (63 MHz, $CDCl_3$): δ= 165.8 (C), 161.3 (C), 136.4 (C), 136.3 (C), 133.6 (C), 129.8 (CH), 129.3 (2 CH), 129.0 (2 CH), 128.9 (2 CH), 128.5 (CH), 125.1 (2 CH), 104.2 (CH), 68.9 (C), 48.9 (CH), 31.2 (CH_2), 8.6 ppm (CH_3); IR(KBr): 2140 (m), 1684 (s), 1655 (m), 1460 (m), 760 (m), 702 (m); *trans*-12r: MP 180-183 ºC (decomposes); ^{1}H NMR (250 MHz, $CDCl_3$): δ= 7.69 (bs, 1H), 7.51-7.34 (m, 10H), 5.63 (dd, *J* = 1.8, 3.0 Hz, 1H), 4.34 (d, *J* = 3.3 Hz, 1H), 2.14-2.00 (m, 1H), 1.57-1.42 (m, 1H), 1.02 ppm (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (63 MHz, $CDCl_3$): δ= 166.0 (C), 160.3 (C), 137.1 (C), 135.7 (C), 133.7 (C), 129.9 (2 CH), 129.8 (CH), 129.3 (2 CH), 128.7 (2 CH), 128.5 (CH), 125.1 (2 CH), 105.2 (CH), 67.9 (C), 49.5 (CH), 24.6 (CH_2), 8.0 ppm (CH_3); IR(KBr): 2144 (m), 1691 (s), 1657 (m), 1496 (w), 1470 (w), 1455 (w), 1372 (w), 1321 (w), 1289 (w), 1276 (w), 1155 (w), 985 (w), 761 (m), 698 (m); HRMS

(EI, 70 eV): calculated for $C_{20}H_{18}N_2O$ (M^+, mixture of diastereomers) 302.1414, found 302.1421.

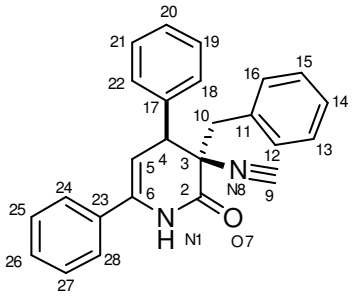
3,4-Dihydropyridin-2-one 12s: According to General procedure I, reaction between phosphonate **1a**, *n*BuLi, benzonitrile **2a**, benzaldehyde **3b** and isocyanoacetate **11e**, followed by column chromatography (*c*-hexane/ EtOAc = 9:1→8:2) afforded **12s** at rt as a yellow solid (32 mg, 0.10 mmol, 10%) and at reflux as a pink solid (93 mg, 0.29 mmol, 29%). MP 127-130 ºC; ^{1}H NMR (250 MHz, $CDCl_3$): δ= 7.93 (br s, 1H), 7.49-7.26 (m, 10H), 5.65 (dd, *J* = 1.5, 6.8 Hz, 1H), 3.94 (d, *J* = 6.8 Hz, 1H), 2.59-2.46 (m, 1H), 1.23 (d, *J*, 6.75 Hz, 3H), 1.14 ppm (d, *J* = 6.75 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ= 166.5 (C), 161.4 (C), 137.3 (C), 135.9 (C), 133.4 (C), 129.8 (CH), 129.3 (2 CH), 129.0 (4 CH), 128.5 (CH), 125.1 (2 CH), 103.5 (CH), 73.1 (C), 46.6 (CH), 32.2 (CH), 18.1 (CH_3), 16.9 ppm (CH_3); IR(KBr): 2926 (m), 2136 (m), 1697 (s), 1628 (m), 1453 (m), 757 (s), 696 (s); HRMS (EI, 70 eV): calculated for $C_{21}H_{20}N_2O$ (M^+) 316.1570, found 316.1573.

3,4-Dihydropyridin-2-one 12t: According to General procedure I, reaction between phosphonate **1a**, *n*BuLi, benzonitrile **2a**, benzaldehyde **3b** and isocyanoacetate **11f**, followed by column chromatography (*c*-hexane/EtOAc = 9:1→8:2) afforded **12t** at rt as a yellow solid (155 mg, 0.47 mmol, 47%, *cis*:*trans* = 59:41)[3] and at reflux as a orange solid (183 mg, 0.55 mmol, 55%, *cis*:*trans* = 77:23). ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.65 (br s, 1H, major), 7.58 (br s, 1H, minor), 7.48-7.28 (m, 10H + 10H), 5.65 (dd, *J* = 2.0, 6.8 Hz, 1H, major), 5.61 (dd, *J* = 2.0, 3.2 Hz, 1H, minor), 4.34 (d, *J* = 3.2 Hz, 1H, minor), 3.76 (d, *J* = 6.8 Hz, 1H, major), 2.27-2.22 (m, 1H, major), 2.14-2.08 (m, 1H, major), 2.05-1.99 (m, 1H, minor), 1.93-1.86 (m, 1H + 1H, major and minor), 1.35-1.28 (m, 1H, minor), 1.09 (d, *J* = 6.4 Hz, 3H, major), 1.04 (d, *J* = 6.8 Hz, 3H, major), 0.94 (d, *J* = 2.0

Hz, 3H, minor), 0.92 ppm (d, J = 2.0 Hz, 3H, minor); ^{13}C NMR (101 MHz, $CDCl_3$): δ= 166.7 (C, minor), 166.3 (C, major), 161.7 (C, major), 160.9 (C, minor), 137.3 (C), 136.5 (C), 136.0 (C), 135.6 (C), 133.7 (2 C), 130.2-128.6 (16 CH), 125.1 (2 CH + 2 CH, major and minor), 105.6 (CH, minor), 104.2 (CH, major), 67.9 (C, major), 66.7 (C, minor), 50.5 (CH, minor), 50.4 (CH, major), 46.6 (CH_2, major), 39.3 (CH_2, minor), 25.0 (CH, major), 24.5 (CH_3, major), 24.4 (CH, minor), 24.2 (CH_3, minor), 24.1 (CH_3, minor), 23.9 ppm (CH_3, major); IR (KBr): 2139 (m), 1696 (s), 1658 (m), 1454 (m), 758 (s), 698 (s); HRMS (EI, 70 eV): calculated for $C_{22}H_{22}N_2O$ (M^+) 330.1727, found 330.1724.

3,4-Dihydropyridin-2-one 12u: According to General procedure I, reaction between phosphonate **1a**, *n*BuLi, benzonitrile **2a**, benzaldehyde **3b** and isocyanoacetate **11g**, followed by column chromatography (*c*-hexane/ EtOAc = 9:1→8:2) afforded **12u** at rt as a yellow solid (227 mg, 0.62 mmol, 62%, *cis*:*trans* = 63:37) and at reflux as a pink solid (237 mg, 0.65 mmol, 65%, *cis*:*trans* = 83:17). ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.33 (br s, 1H, major), 8.28 (br s, 1H, minor), 7.50-7.20 (m, 15H + 15H), 5.75 (br s, 1H, minor), 5.73 (br s, 1H, major), 4.43 (d, J = 2.9 Hz, 1H, minor), 3.71 (d, J = 6.6 Hz, 1H, major), 3.47 (d, J_{AB} = 13.8, 1H, major), 3.30 (d, J_{AB} = 13.8, 1H, major), 3.38 (d, J_{AB} = 13.8 Hz, 1H, minor), 2.70 ppm (d, J_{AB} = 13.8 Hz, 1H, minor). ^{13}C NMR (101 MHz, $CDCl_3$): δ= 166.2 (C, major), 165.7 (C, minor), 162.4 (C, major), 161.7 (C, minor), 137.5 (C, minor), 137.0 (C, major), 135.7 (C, major), 135.6 (C, minor), 133.6 (C, minor), 133.4 (2 C, minor and major), 133.0 (C, major), 130.7-127.9 (26 CH), 125.3 (2 CH, major), 125.2 (2 CH, minor), 104.9 (CH, minor), 103.5 (CH, major), 69.0 (C, major), 68.6 (CH, minor), 49.7 (CH, minor), 47.6 (CH, major), 43.3 (CH_2, major), 37.3 ppm (CH_2, minor); IR(KBr): 2136 (m), 1699 (s), 1659 (m), 1454.0 (m), 764 (m), 698 (s); HRMS (EI, 70 eV):

calculated for $C_{25}H_{20}N_2O$ (M^+) 364.1570, found 364.1571. Crystals suitable for X-ray diffraction were obtained by slow diffusion of pentane into a saturated solution of 12u in EtOAc. From this solution containing mixture of diastereomers the *cis*-diastereomer was selectively crystalised.



X-ray crystal structure determination of *cis*-12u:

$C_{25}H_{20}N_2O$, Fw = 364.43, colourless plate, 0.30 x 0.15 x 0.03 mm^3, triclinic, $P\overline{1}$ (no. 2), a = 9.2509(1), b = 10.0044(1), c = 11.2360(2) Å, α = 76.1128(5), β = 80.0207(5), γ = 78.4123(5)°, V = 980.33(2) $Å^3$, Z = 2, D_x = 1.235 g/cm^3, μ = 0.08 mm^{-1}. 24790 Reflections were measured on a Nonius KappaCCD diffractometer with rotating anode (graphite monochromator, λ = 0.71073 Å) up to a resolution of $(\sin\theta/\lambda)_{max}$ = 0.65 $Å^{-1}$ at a temperature of 150(2) K. Intensity integration was performed with HKL2000[4] and the data were merged with the SortAV software[5]. An absorption correction was not considered necessary. 4493 Reflections were unique (R_{int} = 0.049), of which 3248 were observed [I>2σ(I)]. The structure was solved with Direct Methods using the program SHELXS-97[6] and refined with SHELXL-97[6] against F^2 of all reflections. Non hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were located in difference Fourier maps and refined freely with isotropic displacement parameters. 334 Parameters were refined with no restraints. R1/wR2 [I > 2σ(I)]: 0.0383 / 0.0918. R1/wR2 [all refl.]: 0.0593 / 0.1024. S = 1.083. The extinction parameter refined to 0.022(3). Residual electron density between -0.19 and 0.21 e/$Å^3$.

Geometry calculations and checking for higher symmetry was performed with the PLATON program[7].

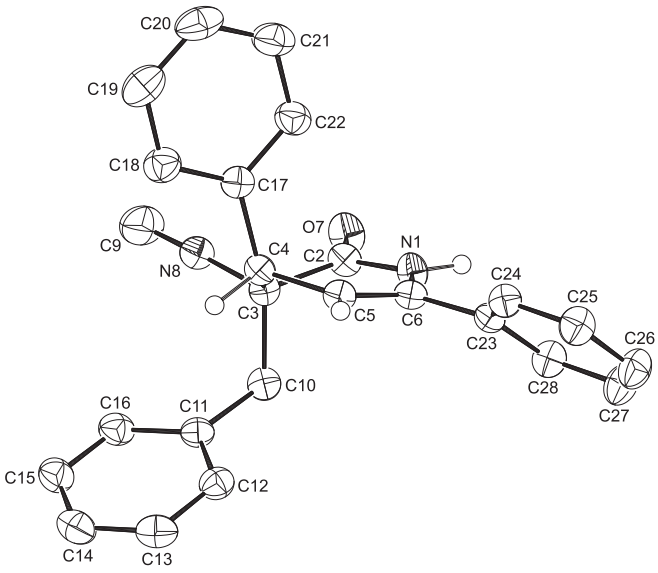


Figure S1. Displacement ellipsoid plot of **12u**, drawn at the 50% probability level. The compound was crystallized by slow diffusion of pentane into a saturated solution of **12u** in EtOAc as a racemate in the centrosymmetric space group $P\overline{1}$. Phenyl- and benzyl-hydrogens are omitted for clarity.

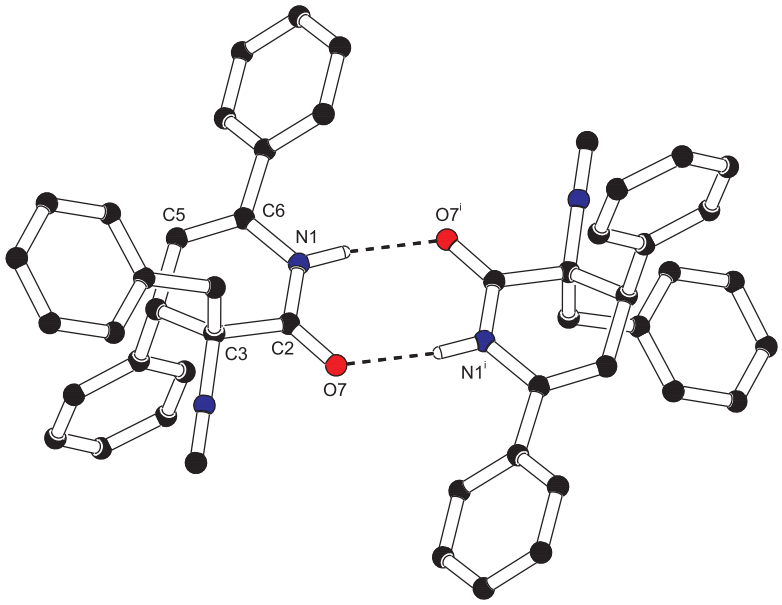


Figure S2. Hydrogen bonding interaction in *cis*-**12u**. C-H hydrogen atoms are omitted for clarity. Symmetry operation i: 1-x, 1-y, 1-z. Distance N1···O7^{i} 2.8848(14) Å.

3,4-Dihydropyridin-2-one 12v: According to General procedure I, reaction between phosphonate **1a**, *n*BuLi, isobutyronitrile **2b**, benzaldehyde **3b** and isocyanoacetate **11g**, followed by column chromatography (*c*-hexane/EtOAc = 9:1→8:2) afforded **12v** at rt as a white solid (67 mg, 0.20 mmol, 20%, *cis*:*trans* = 85:15) and at reflux as a white solid (65 mg, 0.20 mmol, 20%, *cis*). MP 187-190 ºC; ^{1}H NMR (250 MHz, $CDCl_3$)[8]: δ= 7.73 (br s, 1H), 7.43-7.26 (m, 8H), 7.10-7.07 (m, 2H), 5.14 (d, *J* = 6.3 Hz, 1H), 3.47 (d, *J* = 6.3 Hz, 1H), 3.35 (d, J_{AB} = 13.6 Hz, 1H), 3.18 (d, J_{AB} = 13.6 Hz, 1H), 2.47-2.42 (m, 1H), 1.20 (d, *J* = 3.0 Hz, 3H), 1.19 ppm (d, *J* = 3.0 Hz, 3H); ^{13}C NMR (63 MHz, $CDCl_3$): δ= 166.4 (C), 161.9 (C), 142.9 (C), 136.4 (C), 133.1 (C), 130.7 (2 CH), 128.9 (2 CH), 128.8 (2 CH), 128.7 (2 CH), 128.3 (CH), 128.2 (CH), 100.2 (CH), 69.0 (C), 46.9 (CH), 43.2 (CH_2), 31.6 (CH), 20.8 (CH_3), 20.2 ppm (CH_3); IR(KBr): 2139 (m), 2103 (m), 1703 (s),

1674 (m) , 1494 (m), 1454 (m), 1387 (w), 1370 (w), 700(s); HRMS (EI, 70 eV): calculated for $C_{22}H_{22}N_2O$ (M^+) 330.1727, found 330.1726.

3,4-Dihydropyridin-2-one 12w: According to General procedure I, reaction between phosphonate **1a**, *n*BuLi, 2-furonitrile **2c**, benzaldehyde **3b** and isocyanoacetate **11g**, followed by column chromatography (*c*-hexane/EtOAc = 9:1→8:2) afforded **12w** at rt as a white solid (130 mg, 0.37 mmol, 37%, *cis*:*trans* = 81:19) and at reflux as a slightly purple solid* (218 mg, 0.61 mmol, 61%, *cis*:*trans* = 77:23). ^{1}H NMR (250 MHz, $CDCl_3$): δ= 8.89 (br s, 1H, minor), 8.84 (br s, 1H, major), 7.49-7.14 (m, 11H + 11H), 6.56-6.55 (m, 1H, major), 6.50-6.45 (m, 1H (major) + 2H (minor)), 5.87-5.85 (m, 1H + 1H), 4.43 (d, *J* = 2.8 Hz, 1H, minor), 3.71 (d, *J* = 6.5 Hz, 1H, major), 3.44 (d, *J* = 13.6 Hz, 1H, major), 3.37-3.24 (m, 1H + 1H), 2.67 ppm (d, *J* = 14.0 Hz, 1H, minor); ^{13}C NMR (63 MHz, $CDCl_3$): δ= 166.2 (C, major), 165.8 (C, minor), 162.3 (C, major), 161.7 (C, minor), 146.5 (C, minor), 146.4 (C, major), 143.4 (2 CH, minor and major), 135.8 (C, major), 135.5 (C, minor), 133.6 (C, minor), 132.9 (C, major), 130.8-127.9 (20 CH), 128.2 (2 C, major and minor), 112.1 (2 CH, major and minor), 107.7 (CH, major), 107.6 (CH, minor), 102.1 (CH, minor), 101.0 (CH, major), 69.1 (C, major), 68.7 (C, minor), 49.4 (CH, minor), 47.4 (CH, major), 43.4 (CH_2, major), 37.4 ppm (CH_2, minor); IR(KBr): 2137 (m), 1700 (s), 1666 (m), 1495 (m), 1453 (w), 763 (m), 700 (m); HRMS (EI, 70 eV): calculated for $C_{23}H_{18}N_2O_2$ (M^+) 354.1363, found 354.1372.

3,4-Dihydropyridin-2-one 12x: According to General procedure I, reaction between phosphonate **1a**, *n*BuLi, benzonitrile **2a**, 1-cyclohexene-1-carboxaldehyde **3f** and isocyanoacetate **11g**, followed by column chromatography (*c*-hexane/EtOAc = 9:1)

* The difference in appearance is most likely caused by the presence of a minor impurity in the latter case.

afforded **12x** at rt as a white solid (65 mg, 0.18 mmol, 18%, *cis*)[9] and at reflux as a orange solid (181 mg, 0.49 mmol, 49%, *cis*). MP 198-202 ºC (decomposes); ^{1}H NMR (250 MHz, $CDCl_3$): δ= 7.59 (br s, 1H), 7.39-7.20 (m, 10H), 5.48 (br s, 1H), 5.37 (d, *J* = 6.6 Hz, 1H), 3.24 (d, *J* = 13.6 Hz, 1H), 3.06-3.00 (m, 2H), 2.14-1.65 (m, 4H), 1.65-1.47 ppm (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$): δ= 166.9 (C), 161.5 (C), 136.3 (C), 133.8 (C), 133.7 (C), 132.9 (C), 130.7 (2 CH), 129.7 (CH), 129.3 (2 CH), 128.6 (2 CH), 128.5 (CH), 128.2 (CH), 125.1 (2 CH), 102.6 (CH), 67.2 (C), 51.0 (CH), 43.1 (CH_2), 25.6 (CH_2), 24.9 (CH_2), 22.8 (CH_2), 22.0 ppm (CH_2); IR(KBr): 2928 (m), 2134 (s), 1690 (s), 1658 (s), 1467 (s), 1373 (s), 1255 (m), 1092 (m), 756 (s), 699 (s); HRMS (EI, 70 eV): calculated for $C_{25}H_{24}N_2O$ (M^+) 368.1883, found 368.1876.

3,4-Dihydropyridin-2-one 12y: According to General procedure I, reaction between phosphonate **1a**, *n*BuLi, benzonitrile **2a**, *p*-anisaldehyde **3a** and isocyanoacetate **11g**, followed by column chromatography (*c*-hexane/EtOAc = 9:1→8:2) afforded **12y** at rt as a yellow solid (162 mg, 0.41 mmol, 41%, *cis*:*trans* = 71:29) and at reflux as a pink solid (230 mg, 0.58 mmol, 58%, *cis*:*trans* = 83:17). ^{1}H NMR (250 MHz, $CDCl_3$): δ= 7.92 (br s, 1H, major), 7.88 (br s, 1H, minor), 7.53-7.31 (m, 10H + 10H), 7.18 (d, *J* = 7.5 Hz, 2H, minor), 7.10 (d, *J* = 8.5 Hz, 2H, major), 6.98 (d, *J* = 8.5 Hz, 2H, minor), 6.82 (d, *J* = 8.5 Hz, 2H, major), 5.73-5.70 (m, 1H + 1H), 4.37 (d, *J* = 2.8, 1H, minor), 3.86 (s, 3H, minor), 3.76 (s, 3H, major), 3.66 (d, *J* = 6.5 Hz, 1H, major), 3.44 (d, J_{AB} = 13.6, 1H, major), 3.34 (d, J_{AB} = 13.75 Hz, 1H, minor), 3.27 (d, J_{AB} = 13.6, 1H, major), 2.70 ppm (d, J_{AB} = 13.75 Hz, 1H, minor); ^{13}C NMR (63 MHz, $CDCl_3$): δ= 166.0 (C, major), 165.6 (C, minor), 162.2 (C, major), 161.6 (C, minor), 159.9 (C, minor), 159.8 (C, major), 137.3 (C, minor), 136.7 (C, major), 133.7 (C, minor), 133.6 (C, major), 133.0 (2 C, major and

minor), 131.2-127.9 (20 CH), 127.5 (C, minor), 127.4 (C, major), 125.2 (2 CH, major), 125.1 (2 CH, minor), 114.4 (2 CH, major), 114.2 (2 CH, minor), 105.5 (CH, minor), 104.0 (CH, major), 69.1 (C, major), 68.7 (C, minor), 55.5 (CH_3, minor), 55.4 (CH_3, major), 49.1 (CH, minor), 46.8 (CH, major), 43.2 (CH_2, major), 37.3 ppm (CH_2, minor); IR(KBr): 2140 (w), 1711 (s), 1655 (w), 1608 (w), 1511 (s), 1457 (m), 1255 (m), 1178 (w), 1030 (w), 828 (w), 765 (w), 746 (w), 698 (m); HRMS (EI, 70 eV): calculated for $C_{26}H_{22}N_2O_2$ (M^+) 394.1676, found 394.1677.

Computational details

All calculations were performed using the Amsterdam Density Functional (ADF) program developed by Baerends and others,[10,11] and the QUantum-regions Interconnected by Local Descriptions (QUILD) program by Swart and Bickelhaupt.[12] The QUILD program is a wrapper around ADF (and other programs) and is used for its superior geometry optimizer which is based on adapted delocalized coordinates.[12a] The numerical integration was performed using the procedure developed by te Velde *et al.*.[11g,h]

The MOs were expanded in a large uncontracted set of Slater type orbitals (STOs) containing diffuse functions: TZ2P (no Gaussian functions are involved).[11i] The basis set is of triple-ζ quality for all atoms and has been augmented with two sets of polarization functions, i.e. 3*d* and 4*f* on C, N, O and 2*p*, 3*d* on H. The 1*s* core shells of carbon, nitrogen, and oxygen were treated by the frozen-core approximation.[11c] An auxiliary set

of *s*, *p*, *d*, *f* and *g* STOs was used to fit the molecular density and to represent the Coulomb and exchange potentials accurately in each self-consistent field cycle.[11j]

Equilibrium structures were optimized using analytical gradient techniques.[11k] Geometries and energies were calculated at the BP86 level of the generalized gradient approximation (GGA): exchange is described by Slater's Xα potential[11l] with nonlocal corrections due to Becke[11m,n] added self-consistently and correlation is treated in the Vosko-Wilk-Nusair (VWN) parameterization[11o] with nonlocal corrections due to Perdew[11p] added, again, self-consistently (BP86).[11q] Energy minima of all species in Table S1 have been verified to be equilibrium structures through vibrational analysis (i.e., they have zero imaginary frequencies).[13]

Table S1. Proton-affinities (kcal/mol), ε_{HOMO} (eV) and $\%2p_z$(C anion) in THF of different α-acidic esters. [a]

entry	α-acidic ester	Yield (DHP-2-one)	PA (kcal mol^{-1})	ε_{HOMO} (eV)	$\%2p_z$(C anion)
1	**11a**	98%	189	-4.1	35
2	**11d**	31%	199	-3.8	46
3	**11c**	32%	199	-4.0	49
4	**34a**	17%	199	-4.0	51
5	**34b**	7%	184	-4.2	36
6	**34c**	0%	195	-4.1	45

[a] Computed at (COSMO-)BP86/TZ2P.

Solvent effects in water have been estimated using the conductor-like screening model (COSMO), as implemented in the ADF program.[14] For the approach and settings to obtain our solvation *energies* in water, see Ref. [15]. We have verified that our COSMO BP86/TZ2P solvation *free* energies (see Ref.[15]) of methylated DNA bases 9-me-A, 9-me-G, 1-me-C, 1-me-T and 1-me-U (i.e., –12.4, –22.2, –18.6, –11.7, –12.7 kcal

mol^{-1}) agree within ca. one kcal mol^{-1} with the solvation free energies obtained with AMBER/TI by Miller and Kollman[16] (i.e., –12.0, –22.4, –18.4, –12.4, –14.0 kcal mol^{-1}).

Cartesian coordinates and total energies

Table S2. Cartesian coordinates (in Å) and total energies (in a.u.) of gas phase structures in Table 4.[a]

Acid				Base			
MeO*H* (-690.5278)				**MeO$^-$** (-595.4571)			
C	0.061118	-0.020545	0.000034	C	0.121065	-0.004385	-0.000045
O	1.491768	0.010866	-0.000256	O	1.446072	-0.000522	0.000052
H	-0.275083	1.022487	0.001045	H	-0.401773	1.029861	-0.000119
H	-0.344781	-0.515683	-0.897940	H	-0.397188	-0.523820	-0.897083
H	-0.344406	-0.517282	0.897293	H	-0.397324	-0.523766	0.896933
H	1.812767	-0.904744	-0.000900				
1-azadiene*H*$^+$ (-4282.6921)				**1-azadiene** (-4324.6560)			
C	-0.754951	1.166228	-0.473010	C	-0.802287	1.148661	-0.421282
C	-0.325528	2.465208	-0.556210	C	-0.335467	2.407854	-0.553546
C	0.033858	0.092081	0.044319	C	0.009818	0.027153	0.103642
C	-0.577805	-1.169910	0.456596	C	-0.692210	-1.024939	0.892982
N	1.360096	0.202095	0.144168	N	1.279972	-0.103939	-0.094765
C	-1.896354	-1.187640	0.956682	C	-1.952579	-0.794891	1.467803
C	-2.464786	-2.381349	1.387178	C	-2.581703	-1.785698	2.223669
C	-1.736581	-3.572713	1.309952	C	-1.961196	-3.021904	2.410143
C	-0.433371	-3.570981	0.801210	C	-0.704892	-3.260824	1.842028
C	0.145866	-2.379882	0.380797	C	-0.075872	-2.271857	1.091558
H	-2.455928	-0.257705	1.046196	H	-2.436888	0.173764	1.344784
H	-3.476163	-2.384807	1.789646	H	-3.555782	-1.588977	2.670463
H	-2.187989	-4.507452	1.640071	H	-2.453340	-3.797619	2.996884
H	0.123528	-4.502712	0.719473	H	-0.217166	-4.224960	1.984961
H	1.141654	-2.398811	-0.062949	H	0.903452	-2.437173	0.646015
H	1.863214	0.980596	-0.266372	H	1.621761	0.655696	-0.697616
H	-1.758906	0.899991	-0.793541	H	-1.832938	0.917814	-0.695611
C	-1.031280	3.592925	-1.102220	C	-1.039629	3.566250	-1.102290
H	0.649742	2.714441	-0.125934	H	0.675670	2.615448	-0.188217
C	-2.272023	3.477866	-1.775624	C	-2.273330	3.470363	-1.776898
C	-2.902000	4.606190	-2.277300	C	-2.902005	4.606186	-2.277297
C	-2.314389	5.870411	-2.119619	C	-2.315769	5.867438	-2.119990
C	-0.450481	4.876727	-0.960443	C	-0.460359	4.841994	-0.960850
C	-1.087685	6.004052	-1.461627	C	-1.090672	5.980497	-1.460183
H	-2.732420	2.500584	-1.914798	H	-2.735976	2.494452	-1.922891
H	-3.853284	4.511902	-2.798436	H	-3.852909	4.510425	-2.800859
H	-2.815742	6.752346	-2.516707	H	-2.810113	6.754005	-2.516025
H	0.506795	4.974008	-0.447300	H	0.497079	4.933040	-0.445841
H	-0.633299	6.986203	-1.344411	H	-0.623917	6.957053	-1.335615
H	1.899742	-0.491607	0.650459				
***cis*-12q** (-5716.5997)				deprotonated ***cis*-12q** (-5668.3406)			
C	1.110767	-0.195115	-0.573864	C	0.901919	1.689474	1.145085
C	-0.231619	0.481313	-0.457869	C	1.797618	0.659096	0.846145
C	-1.357821	-0.250426	-0.354861	C	1.538179	-0.421020	0.008823
N	-1.245266	-1.654348	-0.288499	N	0.196004	-0.529772	-0.432259
C	-0.099490	-2.360869	-0.022300	C	-0.803401	0.369343	-0.247480
C	1.146529	-1.476501	0.333628	C	-0.353891	1.778605	0.274026

O	-0.059155	-3.581256	-0.041682
H	-2.066370	-2.221372	-0.485506
C	-2.728388	0.292132	-0.284642
C	-3.728422	-0.369261	0.449921
C	-5.019466	0.153469	0.525879
C	-5.334378	1.345101	-0.129245
C	-4.348548	2.009720	-0.864695
C	-3.060727	1.485763	-0.948176
H	-3.486477	-1.279981	0.998445
H	-5.777770	-0.368751	1.108129
H	-6.343189	1.752535	-0.071153
H	-4.588739	2.934579	-1.388225
H	-2.304921	1.990570	-1.548911
C	2.287906	0.743619	-0.373521
C	2.420982	-2.301633	0.143258
H	-0.280863	1.566494	-0.443716
N	1.007818	-1.121954	1.715801
C	0.898961	-0.853082	2.859000
H	1.195212	-0.609310	-1.596859
C	2.331285	1.640177	0.705334
C	3.421753	2.495360	0.875413
C	4.481608	2.476192	-0.034296
C	3.355447	0.737464	-1.282581
C	4.444418	1.595733	-1.117365
H	1.508142	1.667040	1.419337
H	3.440548	3.180887	1.722252
H	5.329452	3.148427	0.097157
H	3.330525	0.056826	-2.135544
H	5.261316	1.579045	-1.838428
H	3.292643	-1.716507	0.457120
H	2.357497	-3.221221	0.732661
H	2.528953	-2.576840	-0.913719

O	-1.979120	0.129500	-0.542177
H	-0.128204	-1.422076	-0.792728
C	2.474931	-1.416697	-0.432034
C	2.124992	-2.436506	-1.367700
C	3.031822	-3.414934	-1.769144
C	4.339743	-3.439801	-1.273801
C	4.714589	-2.437898	-0.360491
C	3.820088	-1.459818	0.045618
H	1.131651	-2.452555	-1.817253
H	2.709111	-4.167688	-2.491360
H	5.047696	-4.205200	-1.590803
H	5.730150	-2.422998	0.040230
H	4.159060	-0.703580	0.752504
N	-1.488221	2.305740	0.990360
C	-2.443386	2.741183	1.518827
C	1.268386	2.732490	2.091886
C	2.264260	2.491398	3.083186
C	2.694643	3.479151	3.961445
C	2.138141	4.765218	3.928862
C	1.131070	5.021307	2.991424
C	0.706386	4.039015	2.100227
H	2.679603	1.488796	3.179497
H	3.459285	3.235059	4.701803
H	2.466080	5.536767	4.625934
H	0.665542	6.007858	2.948924
H	-0.078291	4.294985	1.393552
H	2.799643	0.734236	1.261517
C	-0.144658	2.663515	-0.989791
H	0.136344	3.683084	-0.699752
H	0.673819	2.230812	-1.579847
H	-1.063384	2.687423	-1.591702

***trans*-12q** (-5715.949414)			
C	0.881034	2.226074	0.297162
C	1.892775	1.183412	-0.105674
C	1.635499	-0.135688	-0.019864
N	0.374368	-0.572417	0.439467
C	-0.724525	0.222619	0.646791
C	-0.577497	1.675183	0.086534
O	-1.740187	-0.181290	1.191204
H	0.281296	-1.533867	0.758783
C	2.580085	-1.207854	-0.397069
C	2.116585	-2.390710	-0.999396
C	3.009728	-3.393662	-1.376498
C	4.378821	-3.235165	-1.153517
C	4.849140	-2.066142	-0.548542
C	3.958977	-1.063391	-0.169453
H	1.053360	-2.509772	-1.209563
H	2.633662	-4.297006	-1.855456
H	5.076041	-4.019779	-1.445832
H	5.914688	-1.940563	-0.358736
H	4.326457	-0.166175	0.327836
H	0.956305	3.068986	-0.404464
C	1.147058	2.794485	1.692016
C	1.399594	1.963907	2.794470
C	1.639925	2.508437	4.057108
C	1.649158	3.894338	4.236334
C	1.414374	4.731597	3.143954
C	1.163291	4.183546	1.884068
H	1.420946	0.881000	2.664826
H	1.828839	1.846858	4.902320

deprotonated ***trans*-12q** (-5670.0183)			
C	0.757705	1.537278	1.126979
C	1.734416	0.589791	0.806167
C	1.526085	-0.554502	0.046996
N	0.180975	-0.792642	-0.309996
C	-0.890187	0.007776	-0.085019
C	-0.603593	1.444355	0.459007
O	-2.050349	-0.368462	-0.312985
H	-0.075639	-1.706613	-0.669760
C	2.522610	-1.499507	-0.380775
C	2.205775	-2.651627	-1.159409
C	3.175868	-3.573921	-1.545503
C	4.518052	-3.406004	-1.190485
C	4.860249	-2.270293	-0.435764
C	3.901468	-1.347524	-0.046015
H	1.182997	-2.830945	-1.492521
H	2.874547	-4.436298	-2.143484
H	5.276315	-4.124716	-1.500393
H	5.901331	-2.100382	-0.154066
H	4.217881	-0.475683	0.524887
C	1.108093	2.661016	1.992527
C	2.085707	2.510613	3.014484
C	2.483995	3.571878	3.821888
C	1.915867	4.843329	3.668232
C	0.946183	5.019483	2.673704
C	0.554725	3.962279	1.855156
H	2.511138	1.522120	3.189544
H	3.232915	3.400036	4.597740
H	2.219461	5.672883	4.307526

H 1.846033 4.318723 5.220790 H 1.430441 5.813943 3.270047 H 0.982977 4.844794 1.034658 H 2.851707 1.515221 -0.496044 N -0.786813 1.568683 -1.332675 C -0.975056 1.503274 -2.495136 C -1.663670 2.572881 0.681605 H -1.588123 3.579952 0.252834 H -2.649560 2.153450 0.459131 H -1.545320 2.633187 1.769265	H 0.499412 6.003383 2.518077 H -0.157451 4.157323 1.055695 H 2.746172 0.782228 1.156421 N -0.696957 2.340461 -0.718972 C -0.721747 3.060531 -1.650935 C -1.791960 1.807354 1.374167 H -1.707725 2.834415 1.739525 H -2.727075 1.677064 0.820350 H -1.789181 1.126413 2.234970
***cis*-12u** (-7271.9782) C 0.302034 -0.496693 -0.144554 C -1.167867 -0.690995 -0.427389 C -2.055659 0.296704 -0.209527 N -1.594104 1.501019 0.361089 C -0.399029 1.687708 1.000118 C 0.500596 0.404731 1.121532 O -0.077960 2.763863 1.485210 H -2.195938 2.320321 0.327628 C -3.502314 0.226027 -0.493892 C -4.432587 0.903019 0.314660 C -5.799949 0.818317 0.051171 C -6.262589 0.056660 -1.023244 C -5.346530 -0.618232 -1.835378 C -3.980310 -0.529242 -1.578664 H -4.089973 1.469263 1.181369 H -6.505430 1.341476 0.695715 H -7.330446 -0.008232 -1.229839 H -5.697974 -1.205726 -2.682993 H -3.268669 -1.031202 -2.233263 C 1.062237 -1.817481 -0.139982 C 1.980051 0.807294 1.397524 H -1.505380 -1.653652 -0.801836 N 0.018126 -0.250980 2.304194 C -0.362706 -0.745851 3.304714 H 0.727783 0.118789 -0.959438 C 0.695333 -2.876269 0.706538 C 1.378668 -4.093187 0.661161 C 2.427375 -4.280896 -0.242424 C 2.105173 -2.024395 -1.053462 C 2.784154 -3.243775 -1.105824 H -0.133521 -2.753746 1.402736 H 1.082881 -4.900197 1.331028 H 2.955478 -5.233736 -0.280376 H 2.387051 -1.220430 -1.733890 H 3.589402 -3.382660 -1.827088 H 2.476669 -0.096030 1.773067 H 1.940404 1.531183 2.221987 C 2.792400 1.377635 0.248247 C 2.516086 2.631398 -0.323596 C 3.317372 3.141305 -1.347689 C 4.420206 2.419965 -1.810504 C 3.913711 0.672287 -0.216397 C 4.720987 1.184657 -1.234044 H 1.681594 3.220723 0.053533 H 3.084716 4.116347 -1.775977 H 5.047789 2.823868 -2.605044 H 4.158704 -0.291745 0.230933 H 5.588651 0.618185 -1.572374	deprotonated ***cis*-12u** (-7228.6966) C -0.444099 -0.821386 -0.379446 C 0.870961 -0.954940 0.082079 C 1.922883 -0.099475 -0.207388 N 1.580338 1.026550 -0.985772 C 0.378884 1.321849 -1.533758 C -0.761747 0.268564 -1.385394 O 0.175557 2.382301 -2.146988 H 2.262740 1.770384 -1.096849 C 3.299800 -0.261882 0.183164 C 4.337298 0.591628 -0.292435 C 5.662601 0.441003 0.111230 C 6.037546 -0.568524 1.002874 C 5.034994 -1.431617 1.478214 C 3.713156 -1.285893 1.085350 H 4.118381 1.375090 -1.018678 H 6.416732 1.121481 -0.289084 H 7.075073 -0.686824 1.314838 H 5.294364 -2.232711 2.173071 H 2.970642 -1.973974 1.487007 N -0.941897 -0.283765 -2.748037 C -1.076031 -0.760059 -3.816916 C -2.090896 1.071752 -1.121025 C -1.446602 -1.802621 0.025033 C -1.323950 -2.500654 1.260474 C -2.230973 -3.477287 1.656428 C -3.332255 -3.805425 0.853700 C -3.489270 -3.124359 -0.358222 C -2.575255 -2.153797 -0.764670 H -0.509535 -2.236412 1.934461 H -2.088650 -3.977185 2.616630 H -4.047447 -4.566382 1.166736 H -4.329061 -3.364697 -1.012865 H -2.709583 -1.696721 -1.742101 H 1.099412 -1.835603 0.676830 C -2.146916 1.844223 0.178857 C -1.775569 3.197880 0.225672 C -1.859119 3.924087 1.416454 C -2.316547 3.309803 2.585120 C -2.690707 1.964136 2.551210 C -2.606933 1.239990 1.359879 H -1.400235 3.669151 -0.683276 H -1.562289 4.973824 1.430797 H -2.379575 3.875229 3.516222 H -3.048204 1.471877 3.456528 H -2.901980 0.189886 1.342620 H -2.916991 0.353532 -1.154562 H -2.195699 1.759849 -1.967071
***trans*-12u** (-7270.798394)	deprotonated ***trans*-12u** (-7228.7002)

C	0.554242	1.713133	0.835653
C	1.553294	0.953945	-0.001123
C	1.695259	-0.382219	0.088109
N	0.877848	-1.110086	0.980623
C	-0.157008	-0.583703	1.717673
C	-0.677229	0.787105	1.180168
O	-0.613695	-1.148008	2.698796
H	1.209000	-2.018345	1.299133
C	2.660308	-1.187078	-0.689292
C	2.326095	-2.480839	-1.126319
C	3.233306	-3.235841	-1.870151
C	4.490052	-2.714945	-2.184344
C	4.834626	-1.432330	-1.748497
C	3.930984	-0.676455	-1.004438
H	1.335749	-2.883362	-0.912492
H	2.952324	-4.231279	-2.212293
H	5.199853	-3.306578	-2.761803
H	5.818692	-1.024135	-1.977052
H	4.214879	0.310509	-0.640246
H	0.122073	2.512125	0.216909
C	1.192854	2.388367	2.048559
C	2.033518	1.687635	2.926981
C	2.593174	2.322840	4.036376
C	2.336922	3.675430	4.277044
C	1.518519	4.388478	3.399084
C	0.951191	3.747161	2.295822
H	2.261770	0.637567	2.740151
H	3.236748	1.759558	4.711768
H	2.778889	4.171832	5.140827
H	1.320881	5.446244	3.570820
H	0.313419	4.311639	1.613443
H	2.159186	1.509784	-0.712383
N	-1.350546	0.530967	-0.055709
C	-1.911289	0.357293	-1.079101
C	-1.634294	1.479332	2.191513
C	-3.046668	0.946972	2.329841
C	-4.061006	1.409741	1.478558
C	-5.378866	0.973583	1.628393
C	-5.705892	0.073266	2.644129
C	-4.706350	-0.386082	3.505146
C	-3.388593	0.046068	3.348374
H	-3.818599	2.123172	0.689378
H	-6.150439	1.342885	0.953302
H	-6.734888	-0.264886	2.767544
H	-4.952311	-1.084818	4.304873
H	-2.609949	-0.325504	4.012212
H	-1.688082	2.533445	1.883656
H	-1.127050	1.455160	3.163580
C	1.148658	-0.302369	2.543665
C	-0.235084	-0.265076	2.333352
C	-0.865166	-0.084831	1.111485
N	0.000000	0.000000	0.000000
C	1.353140	0.000000	0.000000
C	2.076025	0.000000	1.381990
O	2.013486	0.012065	-1.051610
H	-0.398581	-0.029429	-0.933595
C	-2.281372	0.043490	0.881262
C	-2.823618	0.379106	-0.393324
C	-4.196635	0.476606	-0.610849
C	-5.111066	0.255149	0.423218
C	-4.602031	-0.066109	1.693424
C	-3.237477	-0.169812	1.917611
H	-2.164153	0.600887	-1.233034
H	-4.555291	0.741598	-1.607395
H	-6.184320	0.335239	0.251865
H	-5.288613	-0.241749	2.523837
H	-2.891148	-0.428832	2.917242
C	1.661209	-0.512592	3.894466
N	2.667688	1.353097	1.495689
C	3.115170	2.435449	1.619871
C	3.323667	-0.951655	1.242451
H	-0.871034	-0.330706	3.212521
C	3.014179	-2.412801	0.999895
C	2.961608	-2.928025	-0.305552
C	2.710338	-4.283631	-0.532401
C	2.507080	-5.151705	0.543535
C	2.558978	-4.651784	1.847222
C	2.810353	-3.296378	2.071921
H	3.101229	-2.244623	-1.143753
H	2.670434	-4.661832	-1.554969
H	2.308157	-6.210114	0.367493
H	2.400998	-5.318130	2.696273
H	2.849676	-2.915049	3.093253
H	3.913652	-0.850963	2.159585
H	3.910275	-0.552465	0.407729
C	0.899953	-1.235546	4.856902
C	1.332702	-1.413750	6.166244
C	2.564474	-0.899431	6.593996
C	2.906855	-0.007175	4.356546
C	3.342790	-0.198886	5.666353
H	-0.038906	-1.693942	4.547307
H	0.708703	-1.980849	6.859955
H	2.907475	-1.044806	7.618528
H	3.521353	0.595227	3.691935
H	4.301430	0.225441	5.970333

[a] Computed at BP86/TZ2P. Total energies are computed with respect to ADF's basic atoms.

Table S3. Cartesian coordinates (in Å) and total energies (in a.u.) of structures in THF solution in Table 4.[a]

Acid				**Base**			
MeO*H* (-693.4782)				**MeO$^-$** (-665.6465)			
C	0.055960	-0.019304	0.000016	C	0.087404	-0.004318	-0.000032
O	1.495571	0.010711	-0.000026	O	1.467594	-0.000561	0.000000
H	-0.282676	1.022254	0.000016	H	-0.381807	1.017894	0.000127
H	-0.338763	-0.520398	-0.896945	H	-0.377340	-0.517848	-0.886319
H	-0.338621	-0.520308	0.897119	H	-0.376483	-0.517969	0.886568
H	1.809961	-0.909116	0.000026				

1-azadiene*H*$^+$ (-4323.0594)	**1-azadiene** (-4330.2344)
C -0.066299 0.280403 -0.118374	C -0.619948 0.911349 -1.375872
C -1.263706 0.846296 0.206727	C -0.432564 2.220297 -1.098555
C 1.199293 0.943803 0.038397	C 0.250138 -0.161503 -0.850020
C 2.452035 0.181457 0.010999	C -0.360223 -1.507439 -0.648908
N 1.268997 2.254069 0.189943	N 1.504881 -0.008036 -0.566410
C 2.469823 -1.164637 0.425821	C -1.749050 -1.664700 -0.501170
C 3.665009 -1.878651 0.434343	C -2.303578 -2.928279 -0.284630
C 4.850291 -1.266630 0.014362	C -1.478238 -4.053834 -0.223534
C 4.840771 0.065920 -0.412914	C -0.093688 -3.909266 -0.373977
C 3.652213 0.788730 -0.412016	C 0.459886 -2.647847 -0.582332
H 1.554334 -1.639792 0.773388	H -2.402344 -0.793392 -0.534175
H 3.673219 -2.913578 0.771173	H -3.381024 -3.031783 -0.162789
H 5.782279 -1.830179 0.013101	H -1.910587 -5.040811 -0.061213
H 5.759466 0.537292 -0.757246	H 0.553476 -4.784771 -0.332931
H 3.649408 1.813171 -0.782685	H 1.535123 -2.526895 -0.701920
H 0.450930 2.848603 0.104590	H 1.804637 0.946720 -0.803332
H -0.021786 -0.732708 -0.508938	H -1.452656 0.598158 -2.006349
C -2.577138 0.261760 0.053052	C -1.208442 3.354726 -1.597239
H -1.265779 1.838329 0.665038	H 0.370839 2.489668 -0.405926
C -2.799109 -0.989658 -0.566715	C -2.219250 3.231933 -2.573783
C -4.087389 -1.496377 -0.680770	C -2.923112 4.350560 -3.011692
C -5.178646 -0.770134 -0.181701	C -2.636628 5.618043 -2.487441
C -3.688348 0.982892 0.546005	C -0.930090 4.637435 -1.083070
C -4.976988 0.470638 0.430924	C -1.636831 5.757332 -1.521088
H -1.961571 -1.560972 -0.964098	H -2.450190 2.255703 -2.998890
H -4.250381 -2.459866 -1.160976	H -3.698062 4.238160 -3.769168
H -6.186091 -1.173870 -0.274515	H -3.188884 6.490505 -2.834924
H -3.524029 1.950072 1.021146	H -0.148891 4.746609 -0.329960
H -5.824158 1.035658 0.815847	H -1.406146 6.738902 -1.108956
H 2.145962 2.708475 0.422423	
***cis*-12q** (-5726.5732)	deprotonated ***cis*-12q** (-5710.1179)
C 1.045401 2.307142 0.333719	C 1.181336 0.728121 2.442381
C 2.015407 1.225864 -0.071978	C -0.205450 0.671549 2.262374
C 1.685412 -0.080631 -0.062342	C -0.849384 0.238603 1.108445
N 0.374423 -0.462501 0.306016	N 0.000000 0.000000 0.000000
C -0.679286 0.384128 0.487811	C 1.348214 0.000000 0.000000
C -0.412854 1.832828 -0.007076	C 2.036309 0.000000 1.403321
O -1.762054 0.015630 0.935754	O 2.019722 -0.067305 -1.047440
H 0.208034 -1.432694 0.566581	H -0.413024 -0.054023 -0.928020
C 2.588706 -1.186999 -0.445468	C -2.265943 0.033310 0.930880
C 2.080042 -2.358317 -1.036178	C -2.813202 -0.494427 -0.274765
C 2.936974 -3.390396 -1.423822	C -4.186735 -0.668340 -0.445503
C 4.314601 -3.272285 -1.224678	C -5.089465 -0.333775 0.569853
C 4.830018 -2.114645 -0.630744	C -4.573367 0.178370 1.773116
C 3.976713 -1.083769 -0.240263	C -3.207624 0.355390 1.953077
H 1.010821 -2.456859 -1.222488	H -2.160534 -0.797711 -1.093060
H 2.524624 -4.285324 -1.887956	H -4.553153 -1.078848 -1.387321
H 4.982981 -4.078546 -1.524838	H -6.161409 -0.471725 0.434719
H 5.901579 -2.019734 -0.459609	H -5.251788 0.442757 2.585251
H 4.384965 -0.197461 0.243908	H -2.855786 0.752986 2.903995
H 1.215055 3.182168 -0.309192	N 3.307840 0.656589 1.198366
N -1.375635 2.697861 0.587374	C 4.350972 1.155500 1.002240
C -2.183480 3.425684 1.030777	C 1.748163 1.274970 3.669476
C 1.252477 2.777214 1.774170	C 1.004943 2.203913 4.456140
C 1.436825 1.872396 2.831063	C 1.482911 2.703180 5.664135
C 1.617449 2.331459 4.138277	C 2.744423 2.328520 6.149232
C 1.630807 3.704236 4.406014	C 3.510219 1.440438 5.384465
C 1.460828 4.613938 3.358619	C 3.029479 0.926126 4.180400
C 1.271019 4.151496 2.053436	H 0.042069 2.559419 4.090502

H	1.453554	0.799331	2.634732
H	1.755306	1.614225	4.946826
H	1.779214	4.061910	5.424667
H	1.477923	5.685376	3.555436
H	1.139560	4.866873	1.240327
H	3.011935	1.526429	-0.385517
C	-0.634738	1.844016	-1.538337
H	-0.514794	2.868859	-1.911306
H	0.103672	1.198887	-2.028637
H	-1.644885	1.489846	-1.774580

H	0.871994	3.412066	6.224691
H	3.123230	2.727534	7.089598
H	4.496969	1.133103	5.733154
H	3.660298	0.226708	3.638322
H	-0.831388	0.946866	3.108121
C	2.324306	-1.484985	1.764959
H	2.850424	-1.554377	2.723898
H	1.363721	-2.008449	1.855451
H	2.927575	-1.962892	0.981814

***trans*-12q** (-5725.70)

C	0.887477	2.232560	0.294554
C	1.897970	1.190458	-0.109664
C	1.640633	-0.128385	-0.017690
N	0.377729	-0.559198	0.453844
C	-0.715030	0.230859	0.638743
C	-0.569338	1.683419	0.079171
O	-1.746205	-0.167703	1.176002
H	0.288617	-1.520064	0.779342
C	2.580245	-1.206179	-0.392918
C	2.105005	-2.422385	-0.916493
C	2.994605	-3.428914	-1.296869
C	4.371636	-3.240365	-1.154961
C	4.853875	-2.037634	-0.626738
C	3.967953	-1.031067	-0.245240
H	1.034997	-2.575308	-1.056543
H	2.608236	-4.359259	-1.710894
H	5.065542	-4.027047	-1.448905
H	5.925324	-1.887719	-0.499812
H	4.350392	-0.107553	0.187884
H	0.967754	3.080799	-0.398432
C	1.145155	2.790033	1.696741
C	1.412089	1.951640	2.790903
C	1.647888	2.487764	4.059500
C	1.636641	3.873310	4.250993
C	1.386703	4.717963	3.165699
C	1.140834	4.178552	1.899784
H	1.451697	0.870116	2.653906
H	1.850206	1.820526	4.896739
H	1.830257	4.291513	5.238603
H	1.387479	5.799070	3.301669
H	0.950085	4.844782	1.057277
H	2.857605	1.525859	-0.494886
N	-0.772761	1.569291	-1.343237
C	-0.961874	1.502022	-2.501924
C	-1.658119	2.589574	0.656204
H	-1.558234	3.598822	0.239036
H	-2.646637	2.190210	0.409943
H	-1.559704	2.640252	1.746307

deprotonated ***trans*-12q** (-5711.182312)

C	0.741691	1.532577	1.140044
C	1.726586	0.595172	0.803932
C	1.515409	-0.547529	0.043721
N	0.168866	-0.792024	-0.296463
C	-0.891799	0.011892	-0.069582
C	-0.610665	1.442818	0.468502
O	-2.061726	-0.358084	-0.310789
H	-0.081481	-1.699066	-0.681670
C	2.516505	-1.497238	-0.387167
C	2.188687	-2.685783	-1.099206
C	3.165255	-3.601752	-1.490864
C	4.516647	-3.384820	-1.201302
C	4.866712	-2.214072	-0.508106
C	3.901012	-1.295402	-0.115729
H	1.155767	-2.913045	-1.362824
H	2.860749	-4.497626	-2.033324
H	5.277717	-4.098850	-1.513181
H	5.913499	-2.011373	-0.278343
H	4.221552	-0.393058	0.402726
C	1.095986	2.655363	2.014096
C	2.070441	2.491211	3.035810
C	2.481007	3.550008	3.843524
C	1.926560	4.827270	3.685422
C	0.958916	5.016678	2.691336
C	0.555943	3.960685	1.873183
H	2.491696	1.500894	3.210464
H	3.228080	3.371789	4.618069
H	2.239318	5.653310	4.323516
H	0.520962	6.003695	2.538412
H	-0.162742	4.164860	1.081887
H	2.737715	0.783360	1.158953
N	-0.671325	2.325544	-0.747920
C	-0.615859	2.999530	-1.710604
C	-1.811236	1.845679	1.345902
H	-1.712343	2.871631	1.708560
H	-2.738410	1.748734	0.772936
H	-1.855412	1.169259	2.209123

***cis*-12u** (-7282.1051)

C	0.000000	0.000000	0.000000
C	1.506044	0.000000	0.000000
C	2.240512	0.508718	-1.005741
N	1.588953	0.990005	-2.164984
C	0.269239	0.864006	-2.460421
C	-0.565120	0.000000	-1.467816
O	-0.236000	1.354911	-3.469198
H	2.130438	1.540752	-2.828326
C	3.715965	0.598258	-1.020871
C	4.433482	0.539964	-2.229521

deprotonated ***cis*-12u** (-7269.6947)

C	0.485171	-0.882793	0.419558
C	-0.832838	-1.004707	-0.039299
C	-1.875443	-0.135109	0.243020
N	-1.530053	0.975323	1.042002
C	-0.339401	1.230151	1.621114
C	0.818845	0.217192	1.404387
O	-0.151370	2.233343	2.340382
H	-2.247882	1.659020	1.268585
C	-3.240623	-0.250931	-0.219298
C	-4.197624	0.789543	-0.049273

C	5.827586	0.615942	-2.236632
C	6.530905	0.751971	-1.037286
C	5.827526	0.816161	0.170824
C	4.435275	0.746444	0.179552
H	3.906801	0.402795	-3.173492
H	6.363876	0.561985	-3.183276
H	7.618620	0.814184	-1.042988
H	6.365826	0.935512	1.110332
H	3.896712	0.826922	1.123053
H	-0.348534	-0.943260	0.443661
N	-1.895261	0.517210	-1.481595
C	-3.013549	0.872540	-1.532180
C	-0.699920	-1.458391	-2.057435
C	-0.539410	1.116429	0.900326
C	-0.103869	2.444194	0.768928
C	-0.599322	3.442504	1.610804
C	-1.526465	3.124225	2.609371
C	-1.957208	1.802987	2.755807
C	-1.467633	0.807893	1.904131
H	0.637366	2.703769	0.011317
H	-0.253439	4.468916	1.491477
H	-1.905678	3.901582	3.272365
H	-2.673376	1.543494	3.534910
H	-1.808938	-0.221560	2.023820
H	2.004066	-0.402111	0.878670
C	0.545326	-2.304578	-2.191888
C	1.332087	-2.240762	-3.353230
C	2.450069	-3.064278	-3.505314
C	2.793284	-3.973359	-2.500382
C	2.008566	-4.057677	-1.346259
C	0.892435	-3.231550	-1.196424
H	1.055845	-1.554209	-4.155611
H	3.045363	-3.004062	-4.415925
H	3.660539	-4.622264	-2.621453
H	2.260009	-4.774743	-0.565129
H	0.272690	-3.321016	-0.302717
H	-1.423871	-1.963840	-1.404150
H	-1.174722	-1.336904	-3.039754

C	-5.508017	0.667506	-0.512507
C	-5.936952	-0.490992	-1.169121
C	-5.012325	-1.533985	-1.345873
C	-3.707201	-1.423722	-0.881936
H	-3.923368	1.726720	0.435170
H	-6.200842	1.495970	-0.360259
H	-6.960922	-0.584317	-1.528566
H	-5.320219	-2.453699	-1.844856
H	-3.033521	-2.268414	-1.018628
N	1.058540	-0.337947	2.768889
C	1.213826	-0.836498	3.822215
C	2.120733	1.046621	1.092249
C	1.488253	-1.864618	0.002394
C	1.330903	-2.597675	-1.208544
C	2.232818	-3.580972	-1.604819
C	3.361279	-3.877680	-0.827171
C	3.557152	-3.157058	0.355702
C	2.648154	-2.178753	0.761515
H	0.492115	-2.369315	-1.865086
H	2.062300	-4.111404	-2.542691
H	4.069893	-4.643993	-1.139744
H	4.423559	-3.365887	0.984379
H	2.827982	-1.679875	1.710233
H	-1.063872	-1.857597	-0.672212
C	2.065049	1.874482	-0.172733
C	1.811320	3.254465	-0.110175
C	1.788798	4.035874	-1.269805
C	2.020791	3.447865	-2.517221
C	2.278552	2.075300	-2.593678
C	2.300798	1.297802	-1.432087
H	1.628079	3.715818	0.860869
H	1.593127	5.105887	-1.197643
H	2.005711	4.054886	-3.422750
H	2.467465	1.607938	-3.560403
H	2.510688	0.229485	-1.501184
H	2.954260	0.338432	1.036012
H	2.289134	1.700561	1.954574

***trans*-12u** (-7282.442439)

C	0.552904	1.712867	0.837546
C	1.550000	0.959764	-0.005359
C	1.706222	-0.374289	0.093178
N	0.904668	-1.098959	1.007001
C	-0.146615	-0.593693	1.714400
C	-0.670246	0.781149	1.187377
O	-0.638029	-1.172783	2.678287
H	1.237852	-2.011288	1.313997
C	2.667703	-1.181194	-0.687508
C	2.367907	-2.508791	-1.043484
C	3.270032	-3.264629	-1.794796
C	4.487790	-2.710155	-2.196798
C	4.798638	-1.392935	-1.841000
C	3.900086	-0.635861	-1.090639
H	1.413041	-2.948115	-0.755272
H	3.016035	-4.287453	-2.069724
H	5.193790	-3.301637	-2.778684
H	5.752090	-0.957688	-2.137776
H	4.161365	0.379786	-0.795725
H	0.118343	2.515132	0.226749
C	1.193022	2.381588	2.055037
C	2.053356	1.682575	2.916976

deprotonated ***trans*-12u** (-7269.5752)

C	0.541882	-0.853720	0.367497
C	-0.791292	-1.035477	-0.022917
C	-1.859302	-0.225058	0.330897
N	-1.527620	0.888729	1.130845
C	-0.321938	1.193790	1.651745
C	0.872049	0.244330	1.355552
O	-0.146432	2.192672	2.380062
H	-2.266339	1.528838	1.411426
C	-3.239308	-0.401777	-0.062852
C	-4.231945	0.594609	0.158200
C	-5.557307	0.414096	-0.238395
C	-5.966309	-0.762165	-0.875975
C	-5.005954	-1.762368	-1.102374
C	-3.685323	-1.593934	-0.704430
H	-3.974177	1.543724	0.628191
H	-6.277968	1.210673	-0.049661
H	-7.001998	-0.901436	-1.183362
H	-5.297340	-2.695009	-1.587031
H	-2.982267	-2.407937	-0.875511
C	1.569310	-1.774568	-0.123211
N	1.209313	-0.322287	2.694919
C	1.442113	-0.833114	3.727931

C	2.616422	2.314627	4.028135	C	2.113405	1.143624	0.994405
C	2.341436	3.661734	4.285620	H	-1.013064	-1.887123	-0.660911
C	1.501983	4.372194	3.423242	C	1.951736	1.988349	-0.250193
C	0.931886	3.734732	2.317747	C	1.641585	3.354345	-0.148519
H	2.299321	0.638741	2.717466	C	1.520827	4.152413	-1.290666
H	3.277011	1.754186	4.688766	C	1.708830	3.595369	-2.559501
H	2.785882	4.156046	5.149177	C	2.021818	2.237101	-2.675109
H	1.291163	5.425052	3.607788	C	2.142366	1.443034	-1.530989
H	0.280359	4.297085	1.647637	H	1.492351	3.791545	0.839406
H	2.146904	1.522518	-0.718472	H	1.282811	5.211322	-1.188286
N	-1.350902	0.515571	-0.045349	H	1.617099	4.215482	-3.451517
C	-1.919771	0.326118	-1.057508	H	2.177026	1.794129	-3.659185
C	-1.629971	1.472569	2.198046	H	2.394612	0.386362	-1.630933
C	-3.047216	0.950773	2.327193	H	2.977407	0.479786	0.883039
C	-4.053319	1.424211	1.469515	H	2.293210	1.791120	1.859336
C	-5.377420	0.998786	1.610390	C	1.384590	-2.490593	-1.340437
C	-5.719885	0.098949	2.623493	C	2.312691	-3.417674	-1.805675
C	-4.729944	-0.366715	3.494656	C	3.494523	-3.671229	-1.095024
C	-3.406604	0.056484	3.347132	C	2.782298	-2.043736	0.567034
H	-3.801500	2.144096	0.689478	C	3.716522	-2.965547	0.092184
H	-6.142151	1.379246	0.933836	H	0.501275	-2.292850	-1.946620
H	-6.752461	-0.229840	2.739971	H	2.119366	-3.937186	-2.745248
H	-4.988426	-1.058939	4.295872	H	4.223278	-4.393477	-1.461549
H	-2.639912	-0.310645	4.027342	H	2.986764	-1.555218	1.516187
H	-1.675098	2.528219	1.897288	H	4.624504	-3.142245	0.669960
H	-1.127759	1.435793	3.172051				

[a] Computed at COSMO-BP86/TZ2P. Total energies are computed with respect to ADF's basic atoms.

Table S4. Cartesian coordinates (in Å) and total energies (in a.u.) of structures in THF solution in Table 6.[a]

Entry	α-acidic ester				base			
1	**11a** (-3262.2328)				deprotonated **11a** (-3260.1296)			
	C	-1.035843	0.152200	-0.266204	C	-0.401453	0.490856	0.400118
	H	-1.584348	-0.122937	-1.174212	C	0.630250	-0.109316	-0.382275
	C	0.444090	-0.201974	-0.551176	O	0.925929	-1.406613	0.027694
	O	1.086573	-0.625712	0.537652	O	1.243933	0.402957	-1.339260
	O	0.928622	-0.048605	-1.656924	N	-0.943199	-0.261659	1.414963
	N	-1.574461	-0.602652	0.811568	C	-1.437250	-0.870795	2.298963
	C	-2.023254	-1.236311	1.691539	C	1.955114	-2.063236	-0.734900
	C	2.505614	-0.921625	0.365082	H	2.906101	-1.519684	-0.669529
	H	3.038573	-0.015527	0.059425	H	2.059746	-3.056093	-0.287171
	H	2.845250	-1.262390	1.344514	H	1.668804	-2.155657	-1.790228
	H	2.632525	-1.705807	-0.387707	C	-0.932164	1.835232	0.216429
	C	-1.159564	1.661322	-0.044250	C	-1.972838	2.321180	1.053133
	C	-1.002557	2.224640	1.227852	C	-2.498491	3.602567	0.896992
	C	-1.082670	3.610005	1.390947	C	-2.015092	4.462381	-0.096628
	C	-1.312225	4.436184	0.286394	C	-0.988690	4.002494	-0.931534
	C	-1.466104	3.873060	-0.983838	C	-0.455168	2.722725	-0.786011
	C	-1.391527	2.487957	-1.150420	H	-2.371163	1.677458	1.836198
	H	-0.828656	1.584837	2.093312	H	-3.296501	3.932743	1.563269
	H	-0.966223	4.042647	2.383830	H	-2.426332	5.464336	-0.216488
	H	-1.375645	5.516129	0.416354	H	-0.593196	4.652087	-1.713892
	H	-1.651502	4.510440	-1.847345	H	0.339658	2.383123	-1.443291
	H	-1.517055	2.048791	-2.140179				
2	**11d** (-2080.3913)				deprotonated **11d** (-2068.3883)			
	C	-1.032360	0.061605	-0.274073	C	-0.834764	0.238612	0.030806
	H	-1.538406	-0.395076	-1.135973	C	0.491693	-0.024208	-0.352699
	C	0.470218	-0.163471	-0.515709	O	1.105854	-1.037645	0.402741

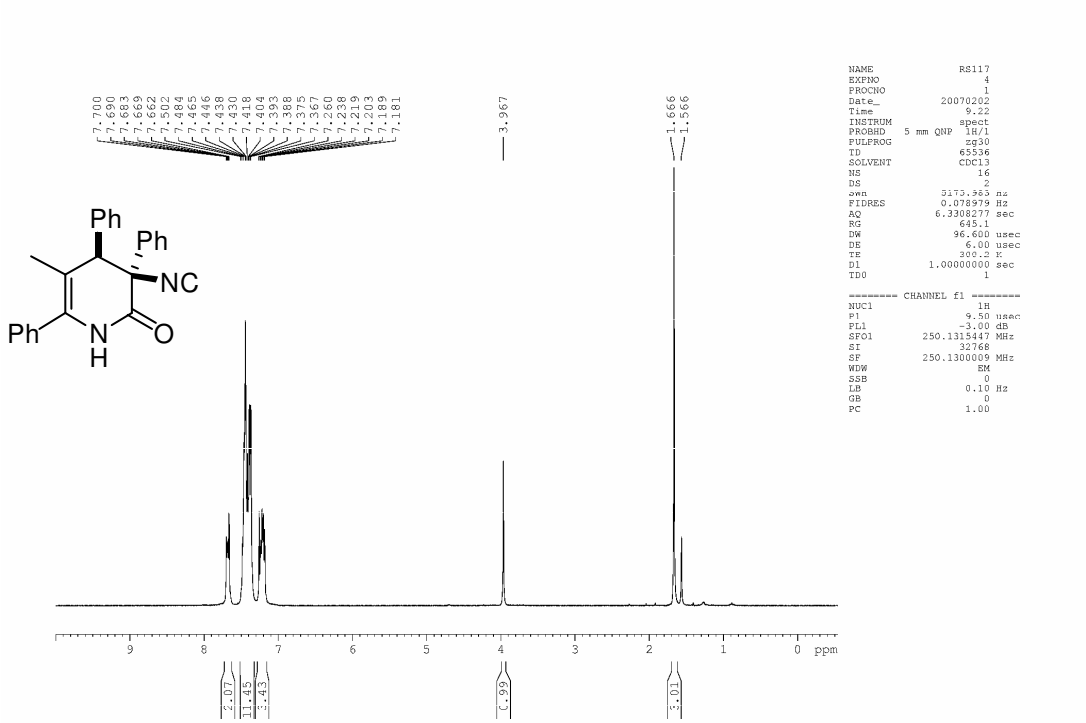
	O 1.077157 -0.819445 0.476217 O 1.010052 0.245511 -1.528851 N -1.517653 -0.592788 0.895974 C -1.951956 -1.108458 1.856259 C 2.504443 -1.059630 0.295404 H 3.035189 -0.105938 0.211994 H 2.816578 -1.602746 1.188996 H 2.667996 -1.660362 -0.604793 C -1.351568 1.566266 -0.238017 H -0.863850 2.043607 0.621086 H -0.988659 2.026231 -1.163217 H -2.434724 1.711132 -0.163429	O 1.132797 0.549099 -1.270638 N -1.413164 -0.462586 1.052253 C -1.975519 -1.031932 1.927083 C 2.461766 -1.331597 0.032771 H 3.111460 -0.454871 0.156093 H 2.784142 -2.129739 0.709708 H 2.528898 -1.677171 -1.007492 C -1.674836 1.288052 -0.649878 H -2.000649 2.081770 0.044048 H -1.080055 1.754632 -1.443771 H -2.585033 0.865204 -1.108383
3	**11c** (-1704.3474) C -1.068175 -0.107485 -0.352999 H -1.547952 -0.624732 -1.193831 C 0.443436 -0.216611 -0.555152 O 1.075606 -0.794855 0.467797 O 0.967322 0.202031 -1.572591 N -1.565399 -0.633734 0.864794 C -1.994079 -1.063887 1.867792 C 2.521456 -0.923622 0.326864 H 2.974675 0.067284 0.223148 H 2.854248 -1.410148 1.245212 H 2.756453 -1.537892 -0.548019 H -1.332375 0.955567 -0.424124	deprotonated **11c** (-1692.0354) C -0.997346 -0.228306 -0.314260 H -1.662707 0.166111 -1.076335 C 0.385217 -0.263572 -0.554556 O 1.128459 -0.795943 0.505791 O 0.961511 0.129394 -1.598202 N -1.569779 -0.670437 0.842617 C -2.095983 -1.046165 1.834664 C 2.549570 -0.841638 0.292148 H 2.963132 0.163367 0.135763 H 2.969156 -1.278117 1.204398 H 2.804417 -1.468806 -0.572249
4	**34a** (-2701.3480) C -1.146484 -0.391002 -0.238916 C 0.353804 -0.625729 -0.398008 O 1.076668 0.392508 0.108248 O 0.840060 -1.626333 -0.900543 C -1.800862 -1.538076 0.537213 C 2.522783 0.247231 0.013607 H 2.824018 0.167998 -1.036175 H 2.932278 1.151391 0.467812 H 2.847190 -0.644244 0.560399 H -1.284323 0.558194 0.298360 H -1.367063 -1.610888 1.542231 H -2.877099 -1.357460 0.631547 H -1.649762 -2.491442 0.017320 C -1.799700 -0.194030 -1.610940 O -2.832673 -0.729227 -1.970877 O -1.095622 0.677514 -2.358959 C -1.637072 0.961542 -3.679950 H -0.939539 1.670494 -4.129916 H -1.689406 0.040287 -4.269647 H -2.635168 1.402723 -3.589682	deprotonated **34a** (-2688.7412) C -0.931260 -0.524372 -0.547679 C 0.475537 -0.303509 -0.604418 O 1.082473 -0.625888 0.629214 O 1.200406 0.108754 -1.532099 C -1.554869 -1.044808 0.734494 C 2.503864 -0.430551 0.671489 H 2.771682 0.618733 0.488154 H 2.812377 -0.721089 1.681480 H 3.018919 -1.056578 -0.069488 H -1.404545 -0.360993 1.585194 H -2.633599 -1.169769 0.588378 H -1.137268 -2.016944 1.040459 C -1.814737 -0.280135 -1.639238 O -3.056627 -0.460209 -1.625752 O -1.220606 0.199089 -2.805168 C -2.129111 0.438719 -3.893597 H -1.505658 0.804863 -4.716125 H -2.644959 -0.481679 -4.197104 H -2.881527 1.193768 -3.630645
5	**34b** (-3663.7288) C -0.681676 0.072663 -0.259942 C 0.692779 -0.245792 0.120199 N 1.782894 -0.495613 0.430816 C -1.704497 -0.543041 0.705151 C -0.954833 -0.413007 -1.703243 O -0.422095 -1.382887 -2.208703 O -1.881697 0.360472 -2.273450 C -2.309287 -0.038055 -3.626781 C -3.366646 0.942623 -4.078873 H -1.423575 -0.026954 -4.272786 H -2.687730 -1.065635 -3.568610 C -1.687550 -1.916724 0.981702	deprotonated **34b** (-3666.0783) C -1.257798 -0.460340 -0.444344 C 0.118365 -0.183232 -0.463775 N 1.274359 0.033525 -0.433195 C -1.834266 -0.980550 0.800327 C -2.002270 -0.211785 -1.646174 O -3.219505 -0.389456 -1.833762 O -1.200594 0.281223 -2.665639 C -1.872709 0.564606 -3.916674 C -0.830559 1.084403 -4.888601 H -2.348036 -0.353410 -4.289311 H -2.665489 1.305679 -3.743013 C -1.010564 -1.183408 1.938779

	C -2.640564 -2.467620 1.841428 C -3.612475 -1.650786 2.428385 C -2.676657 0.273961 1.293239 C -3.628355 -0.280544 2.153667 H -0.929976 -2.557146 0.527846 H -2.621481 -3.535850 2.053450 H -4.353828 -2.081571 3.100763 H -2.688741 1.343632 1.082955 H -4.379950 0.361410 2.611163 H -0.787850 1.164566 -0.241850 H -3.699642 0.664851 -5.087594 H -4.237948 0.923171 -3.411686 H -2.969503 1.965130 -4.117059	C -1.522324 -1.674797 3.137570 C -2.881654 -1.988980 3.260832 C -3.207139 -1.305048 0.945547 C -3.711429 -1.797253 2.150599 H 0.052130 -0.948000 1.873805 H -0.850157 -1.813638 3.985156 H -3.282430 -2.373389 4.198434 H -3.867612 -1.162656 0.095491 H -4.774160 -2.034318 2.219649 H -1.307175 1.311842 -5.851842 H -0.361845 2.002751 -4.510353 H -0.044195 0.337281 -5.060615
6	**34c** (-3883.7954) C -1.113339 -0.036675 -0.370307 C 0.386652 -0.358956 -0.426471 O 1.078813 0.459089 0.384474 O 0.876436 -1.254601 -1.092670 C -1.774016 -0.790066 0.775974 C 2.510563 0.196874 0.469476 H 2.971007 0.315379 -0.516662 H 2.895461 0.939392 1.170553 H 2.683383 -0.818054 0.842282 C -1.723123 -0.341585 -1.745395 O -2.340305 -1.344836 -2.044867 O -1.455652 0.670950 -2.593084 C -1.938490 0.494943 -3.956178 H -1.626939 1.394859 -4.489306 H -1.486675 -0.397858 -4.400832 H -3.029209 0.399809 -3.956798 H -1.211381 1.040086 -0.192453 C -1.724329 -2.189761 0.855883 C -2.332869 -2.855634 1.922975 C -2.994895 -2.131937 2.920225 C -2.436128 -0.069813 1.780062 C -3.045137 -0.737053 2.846678 H -1.210332 -2.759421 0.082661 H -2.288609 -3.943000 1.974156 H -3.468378 -2.653376 3.751824 H -2.476454 1.018848 1.726415 H -3.557843 -0.165055 3.619201	deprotonated **34c** (-3874.9261) C -0.983494 -0.525093 -0.555706 C 0.432905 -0.285396 -0.580419 O 0.999947 -0.342835 0.698342 O 1.171653 -0.026451 -1.547127 C -1.656008 -1.005964 0.681243 C 2.423096 -0.154039 0.744593 H 2.707221 0.844118 0.386422 H 2.698540 -0.262549 1.798623 H 2.946727 -0.907354 0.141731 C -1.818082 -0.315148 -1.706457 O -3.041752 -0.552146 -1.769469 O -1.175975 0.196698 -2.825178 C -2.022567 0.377826 -3.975431 H -1.365371 0.769791 -4.758132 H -2.465479 -0.572849 -4.298593 H -2.829985 1.092247 -3.770030 C -1.152595 -2.093283 1.427883 C -1.791910 -2.551656 2.581622 C -2.970321 -1.943308 3.029506 C -2.845858 -0.410372 1.151099 C -3.492753 -0.868483 2.301359 H -0.240573 -2.585740 1.092622 H -1.371741 -3.396492 3.128962 H -3.473242 -2.302114 3.927768 H -3.267372 0.427981 0.598833 H -4.408387 -0.377848 2.634043

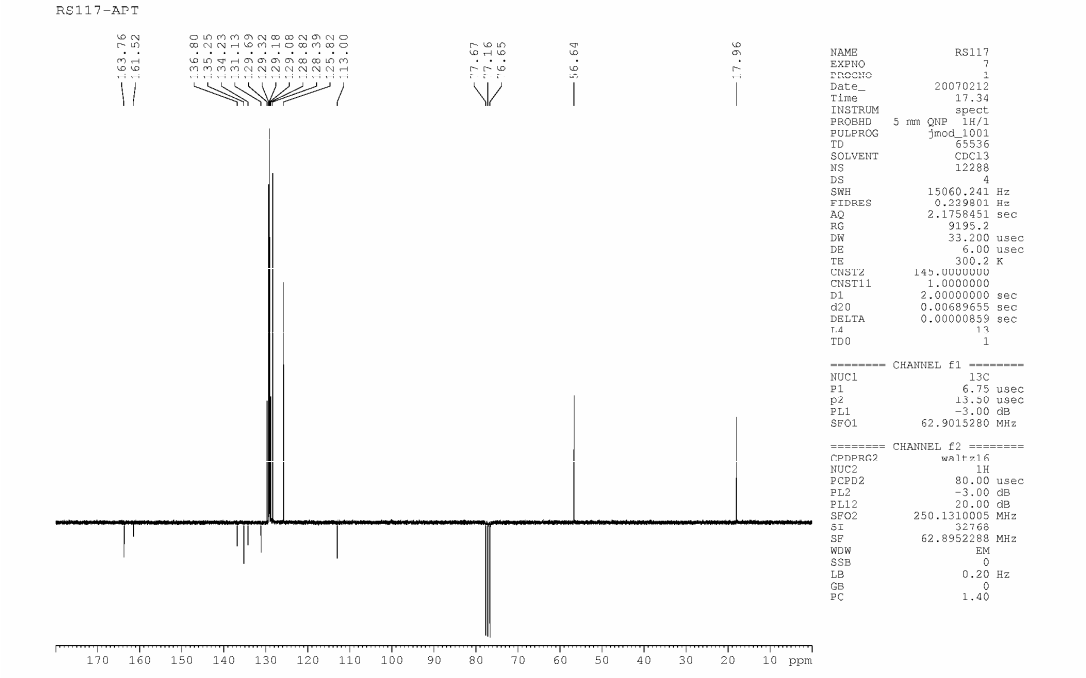
[a] Computed at COSMO-BP86/TZ2P. Total energies are computed with respect to ADF's basic atoms.

^{1}H NMR and ^{13}C NMR spectra of all new compounds

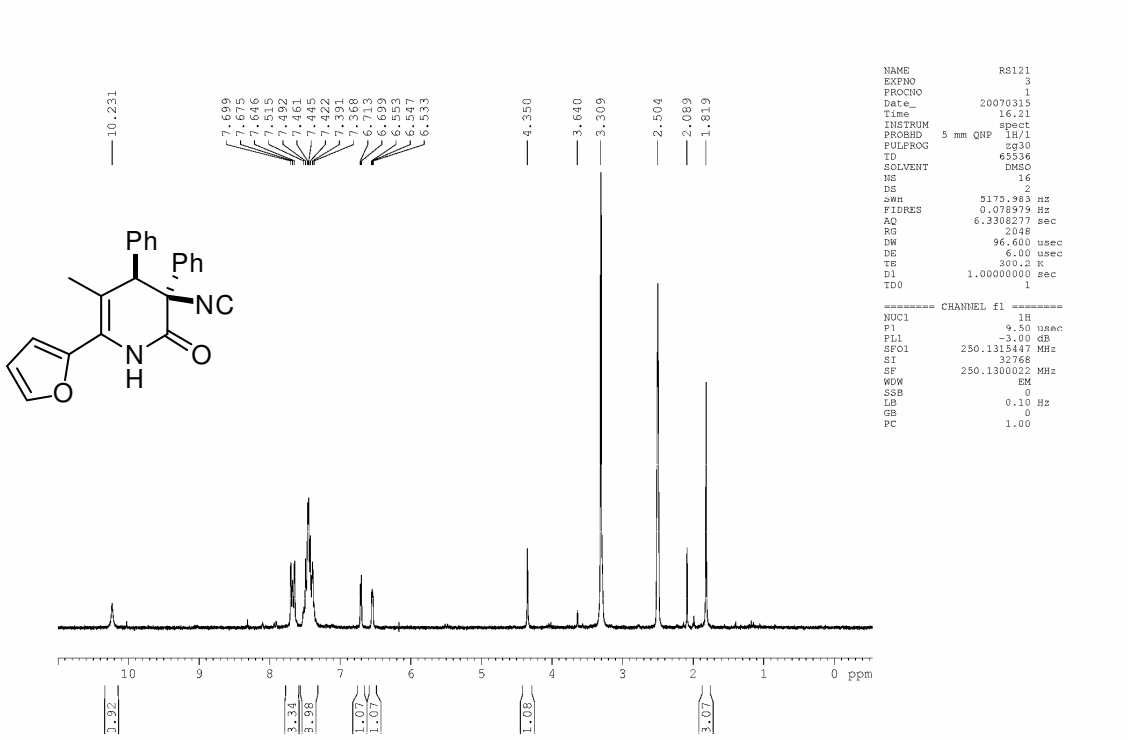
3,4-Dihydropyridin-2-one (**12o**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



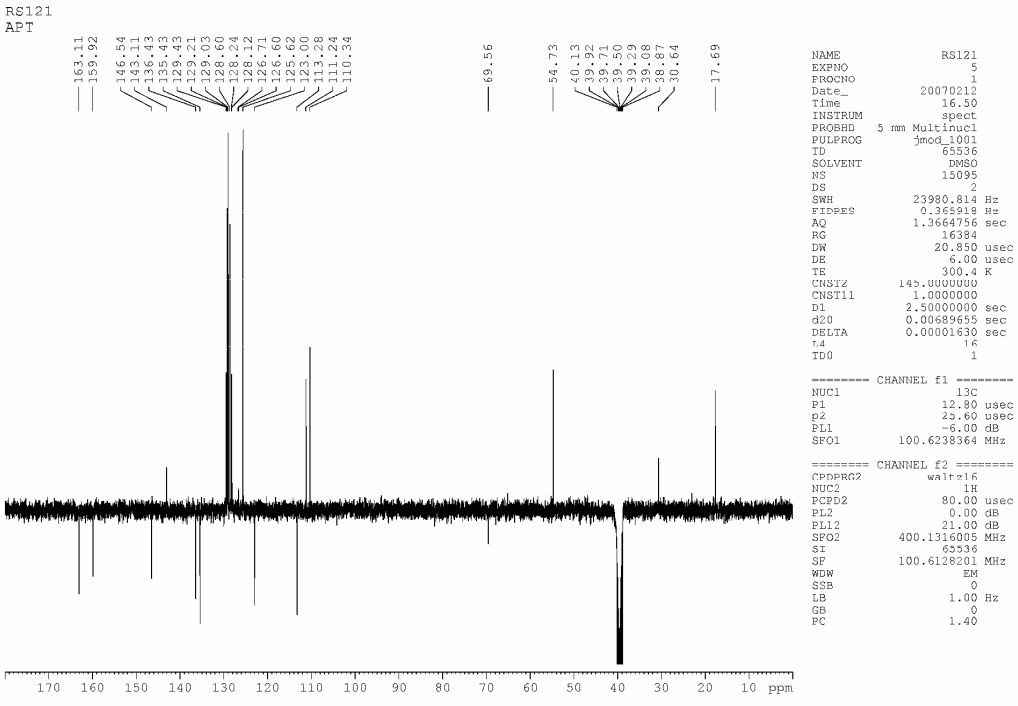
^{13}C{1H} NMR (62.90 MHz, $CDCl_3$)



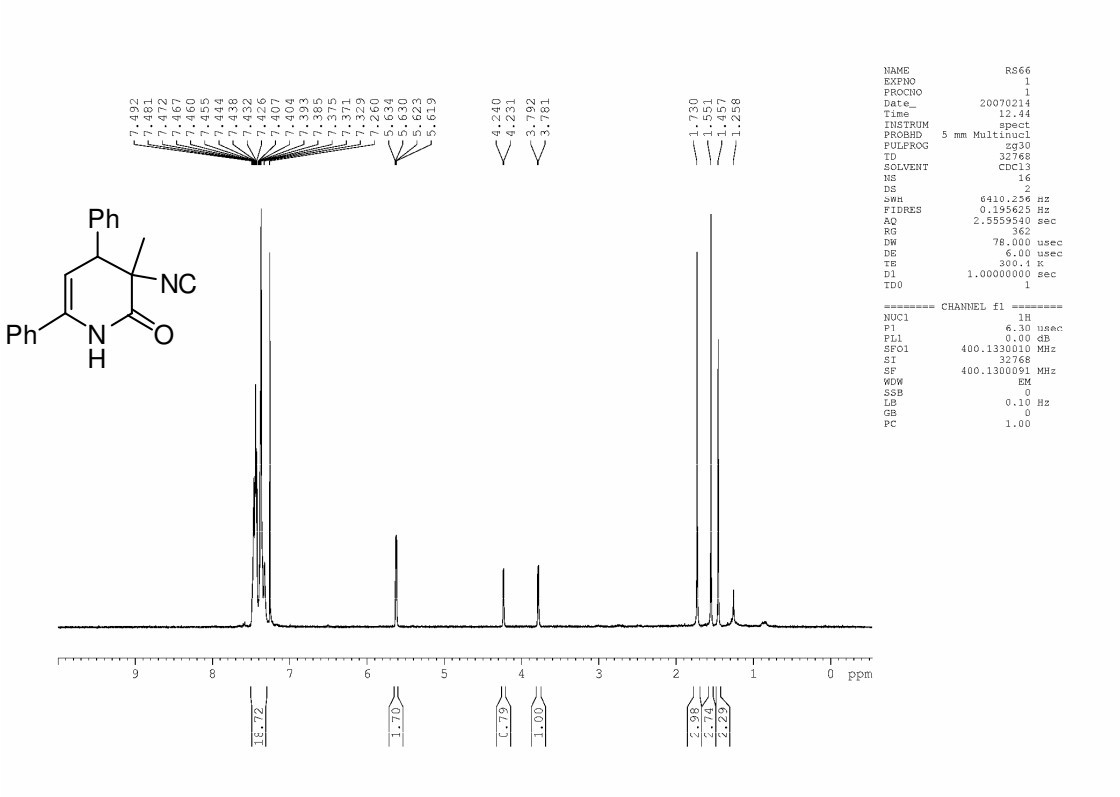
3,4-Dihydropyridin-2-one (**12p**): ^{1}H NMR (250.13 MHz, d^{6}-DMSO)



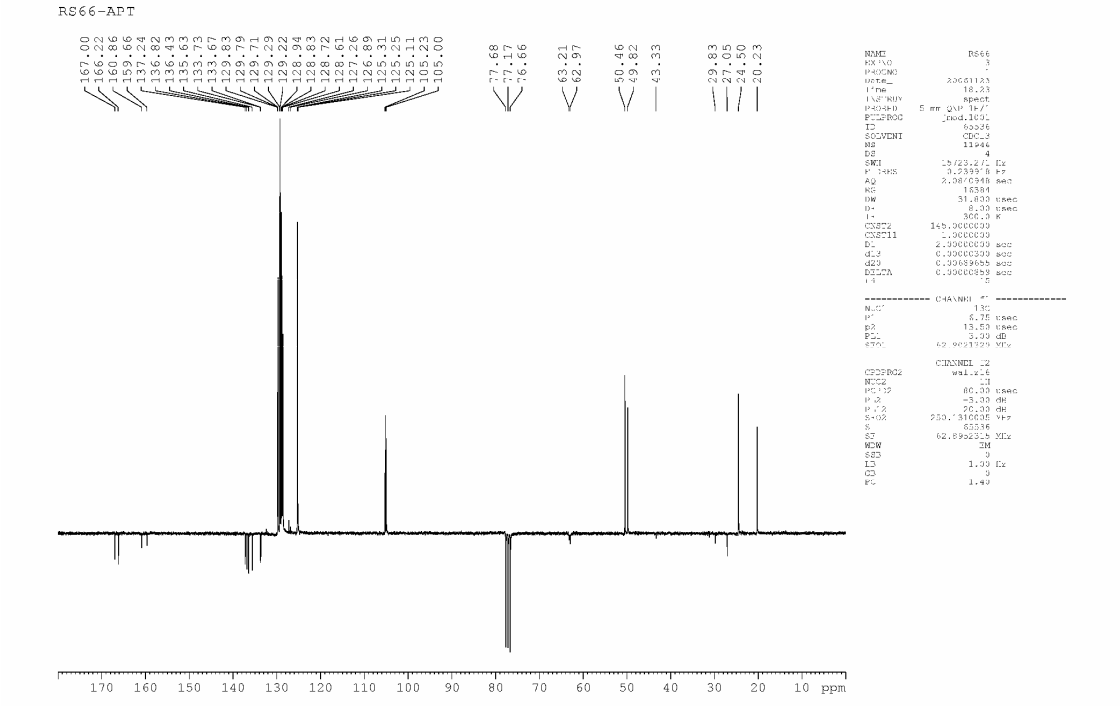
^{13}C{1H} NMR (100.62 MHz, d^{6}-DMSO)



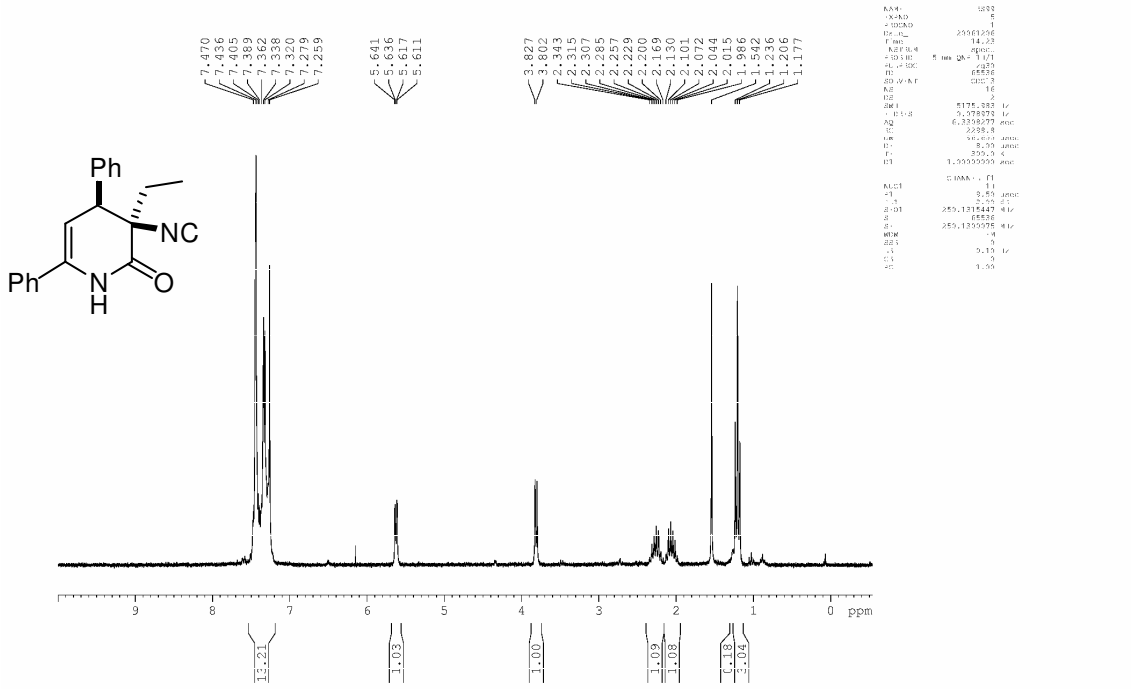
3,4-Dihydropyridin-2-one (**12q**): ^{1}H NMR (400.13 MHz, $CDCl_3$)



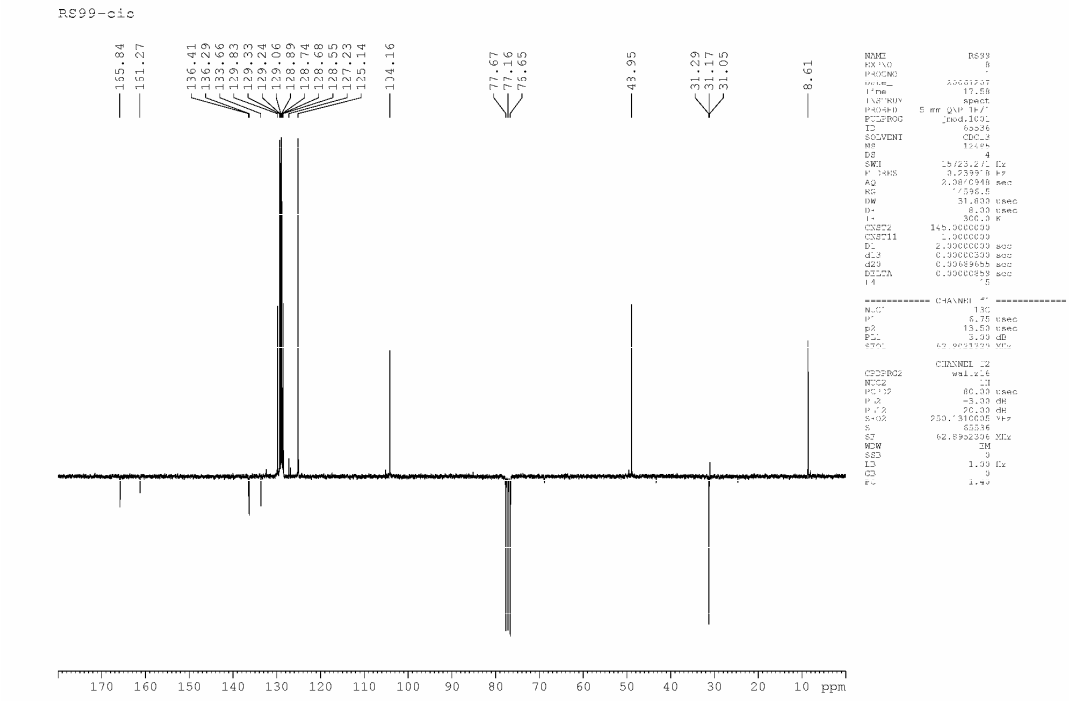
^{13}C{1H} NMR (62.90 MHz, $CDCl_3$)



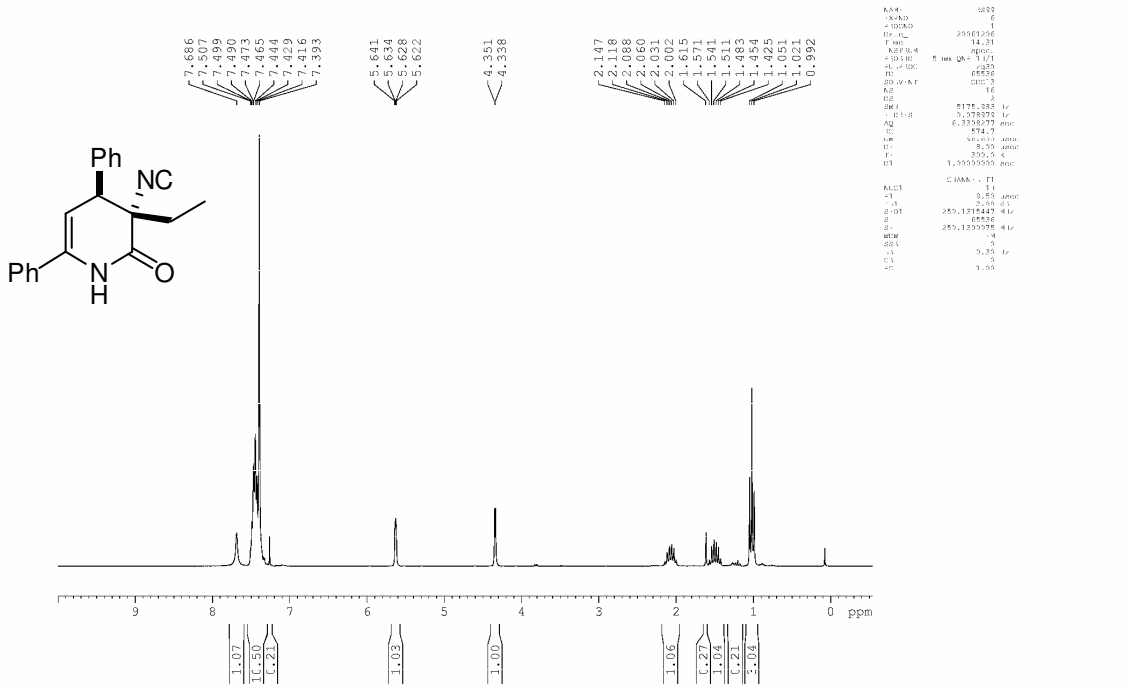
3,4-Dihydropyridin-2-one (**12r-*cis***): ^{1}H NMR (250.13 MHz, $CDCl_3$)



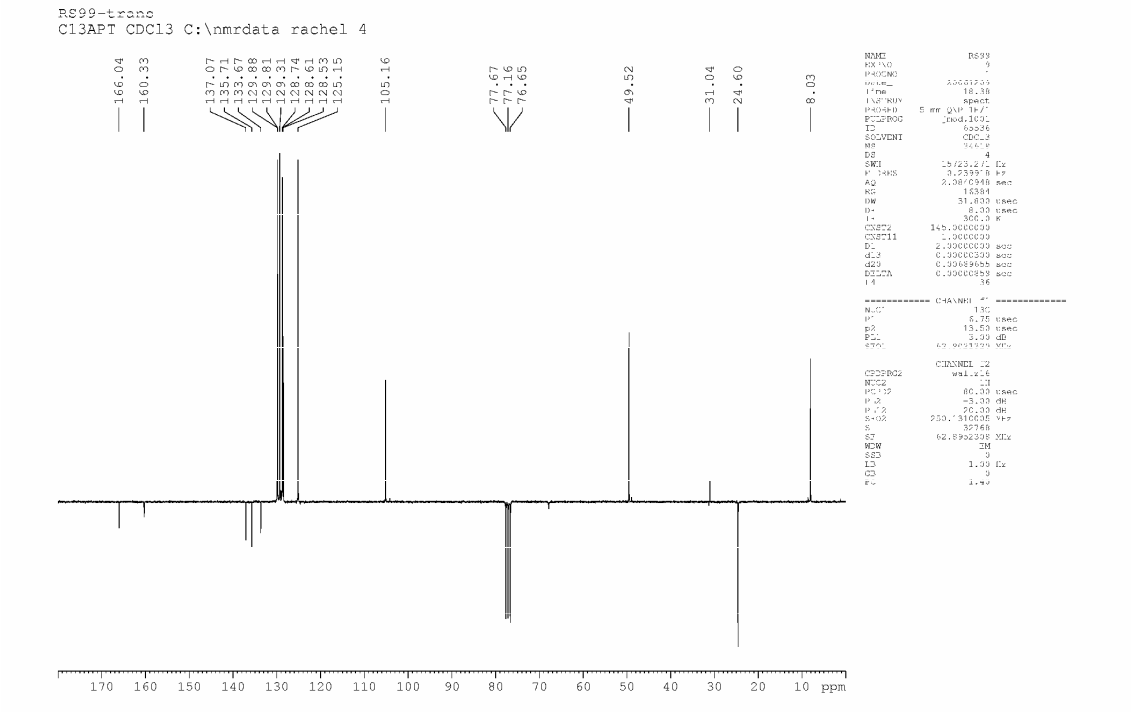
^{13}C{1H} NMR (62.90 MHz, $CDCl_3$)



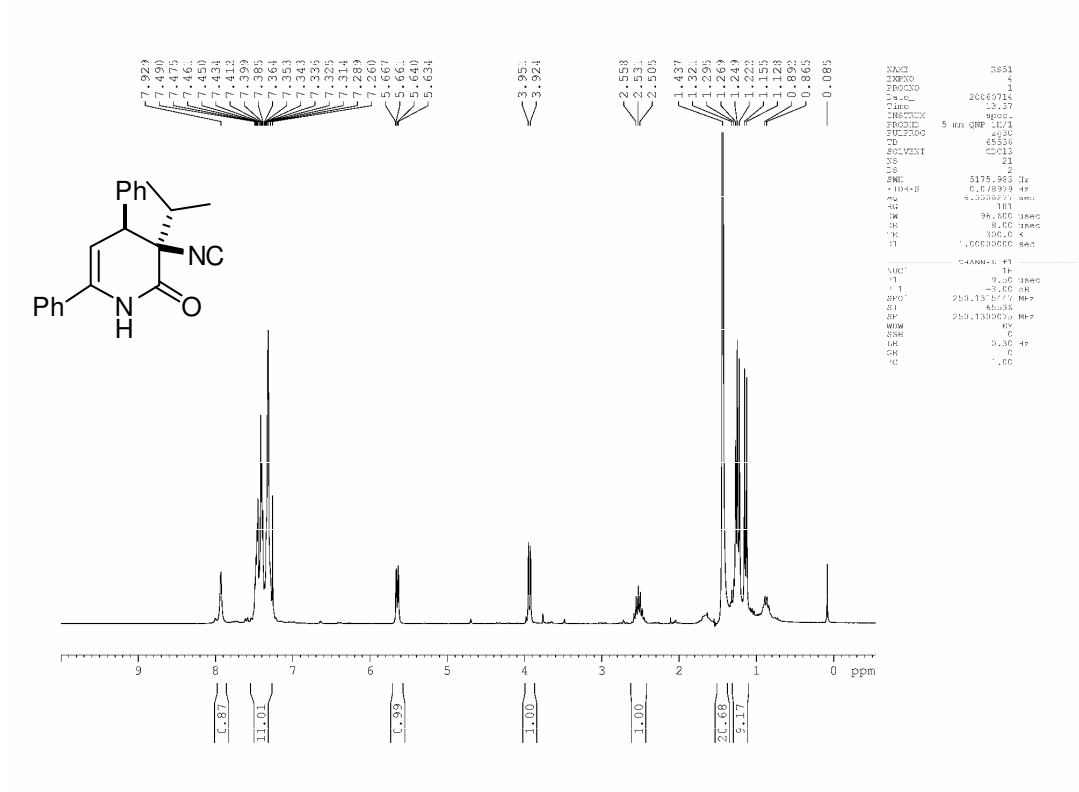
3,4-Dihydropyridin-2-one (**12r-*trans***): ^{1}H NMR (250.13 MHz, $CDCl_3$)



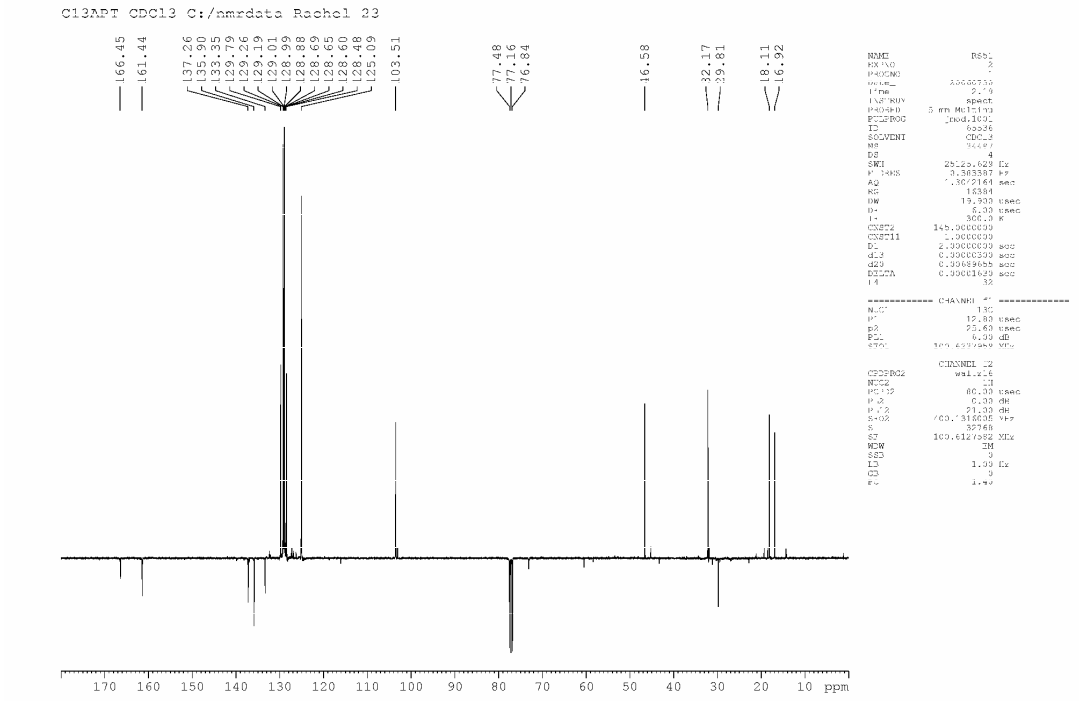
^{13}C{1H} NMR (62.90 MHz, $CDCl_3$)



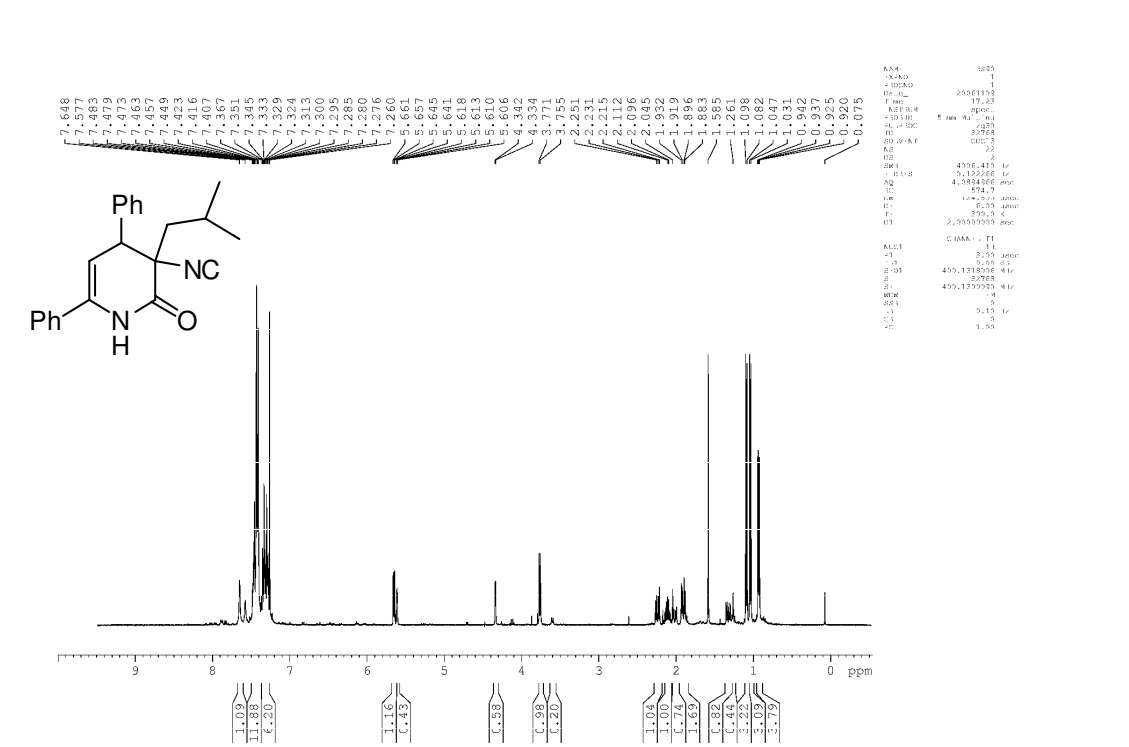
3,4-Dihydropyridin-2-one (**12s**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



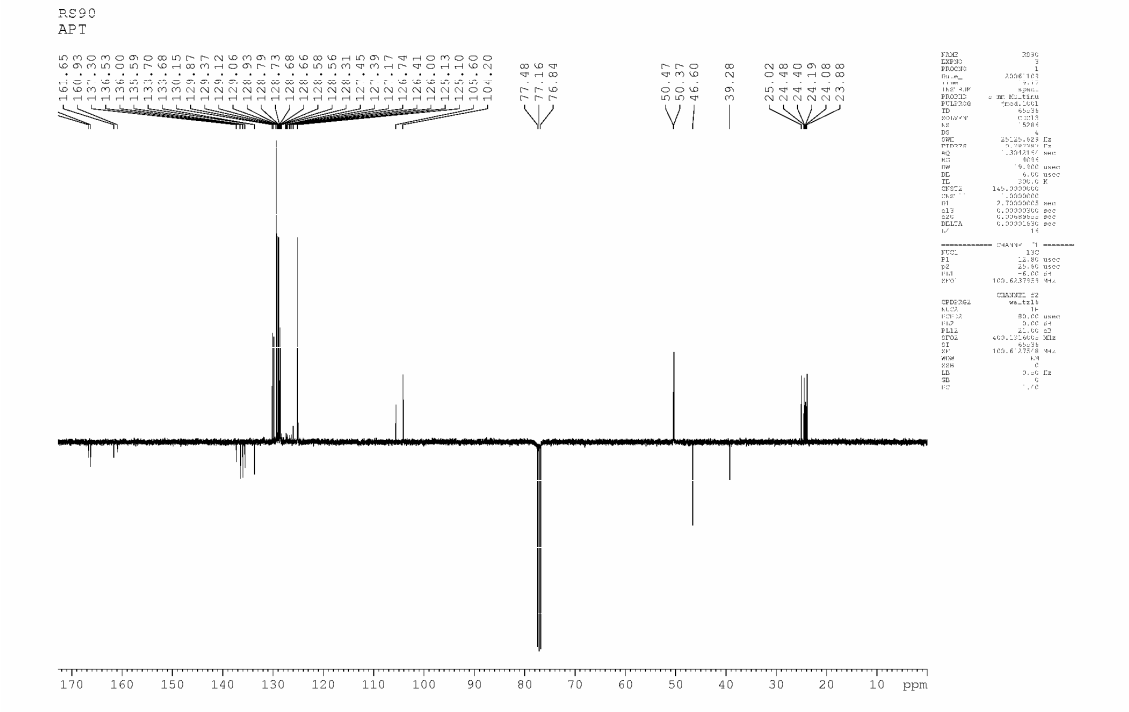
^{13}C{1H} NMR (100.62 MHz, $CDCl_3$)



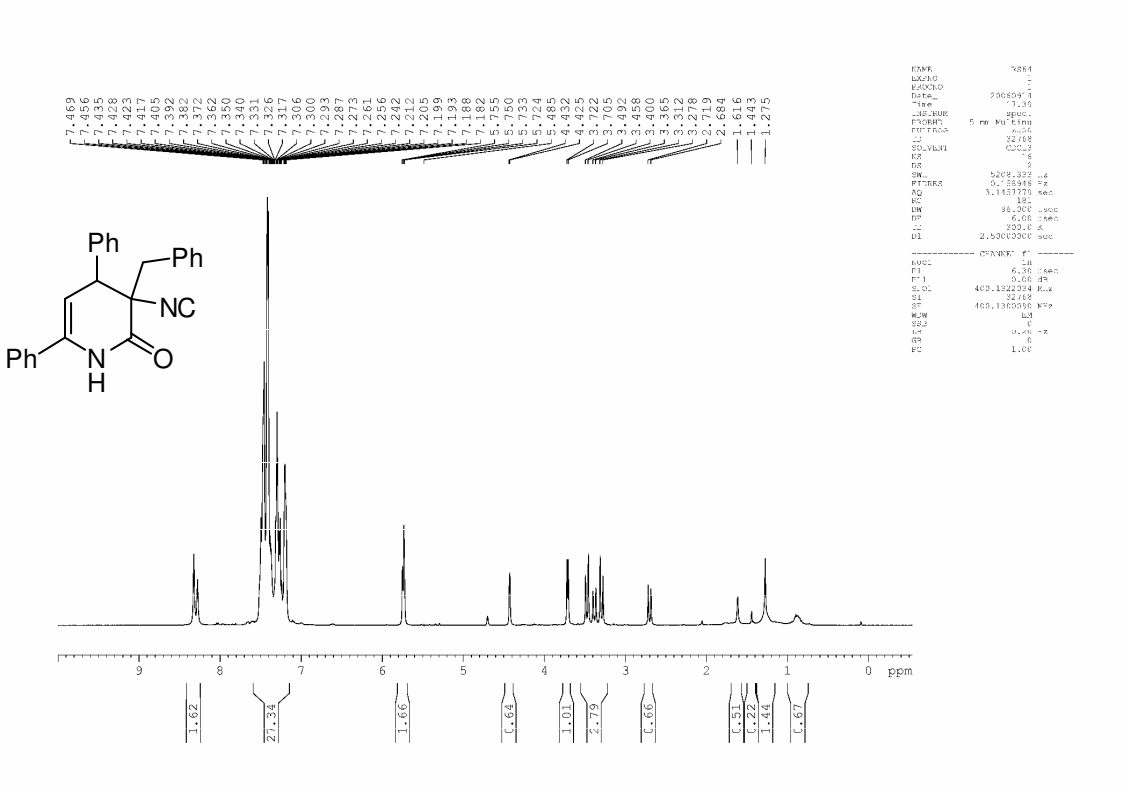
3,4-Dihydropyridin-2-one (**12t**): ^{1}H NMR (400.13 MHz, $CDCl_3$)



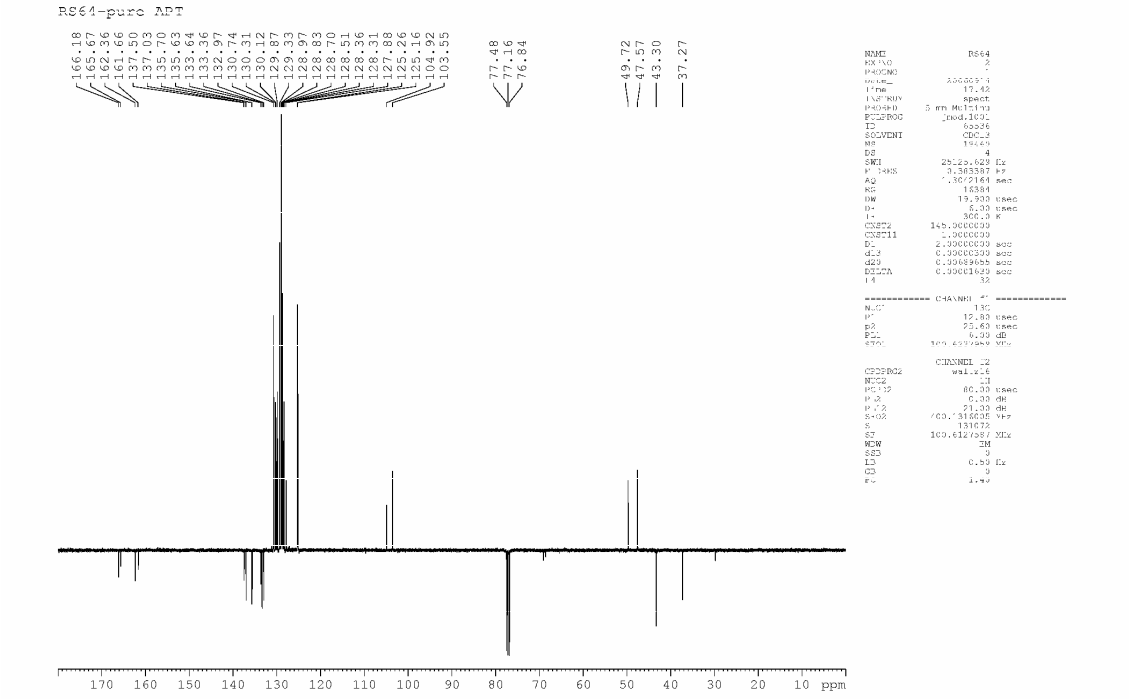
^{13}C{1H} NMR (100.62 MHz, $CDCl_3$)



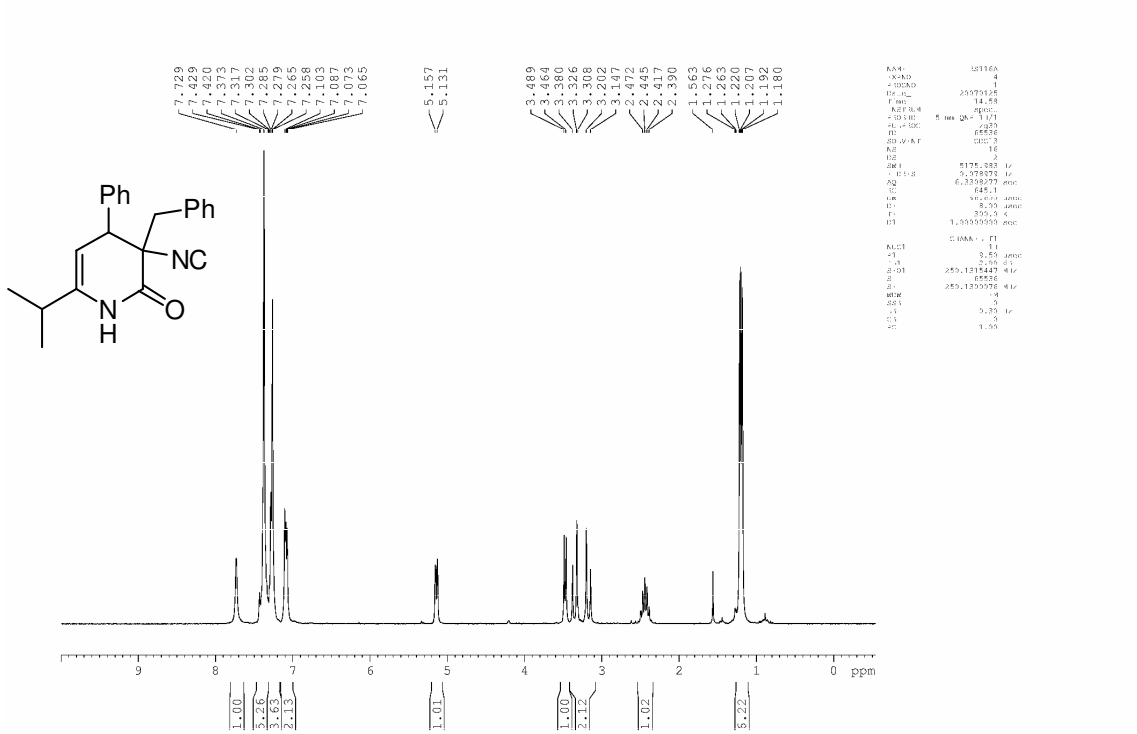
3,4-Dihydropyridin-2-one (**12u**): ^{1}H NMR (400.13 MHz, $CDCl_3$)



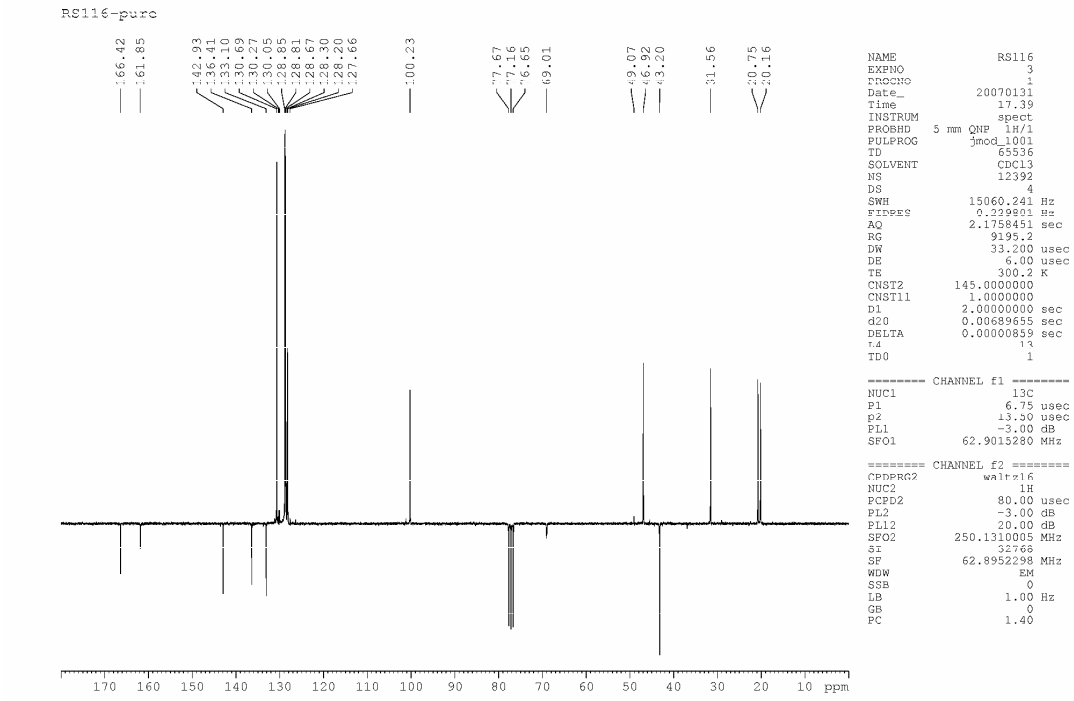
^{13}C{1H} NMR (100.62 MHz, $CDCl_3$)



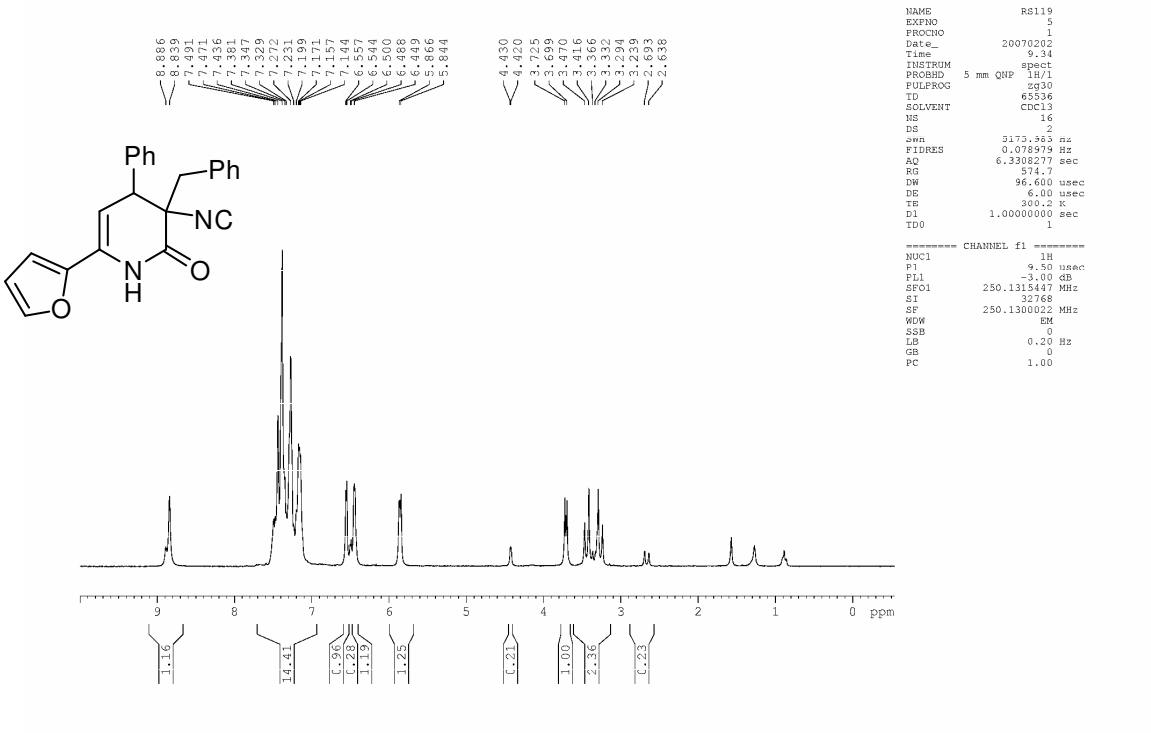
3,4-Dihydropyridin-2-one (**12v**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



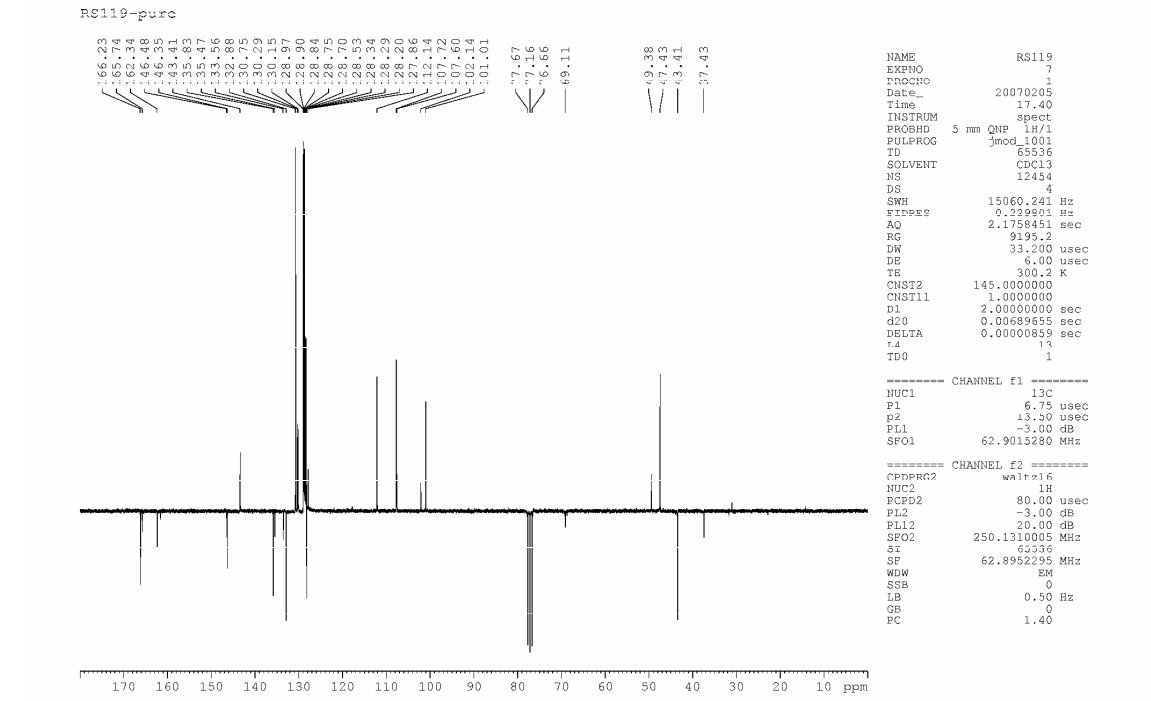
^{13}C{1H} NMR (62.90 MHz, $CDCl_3$)



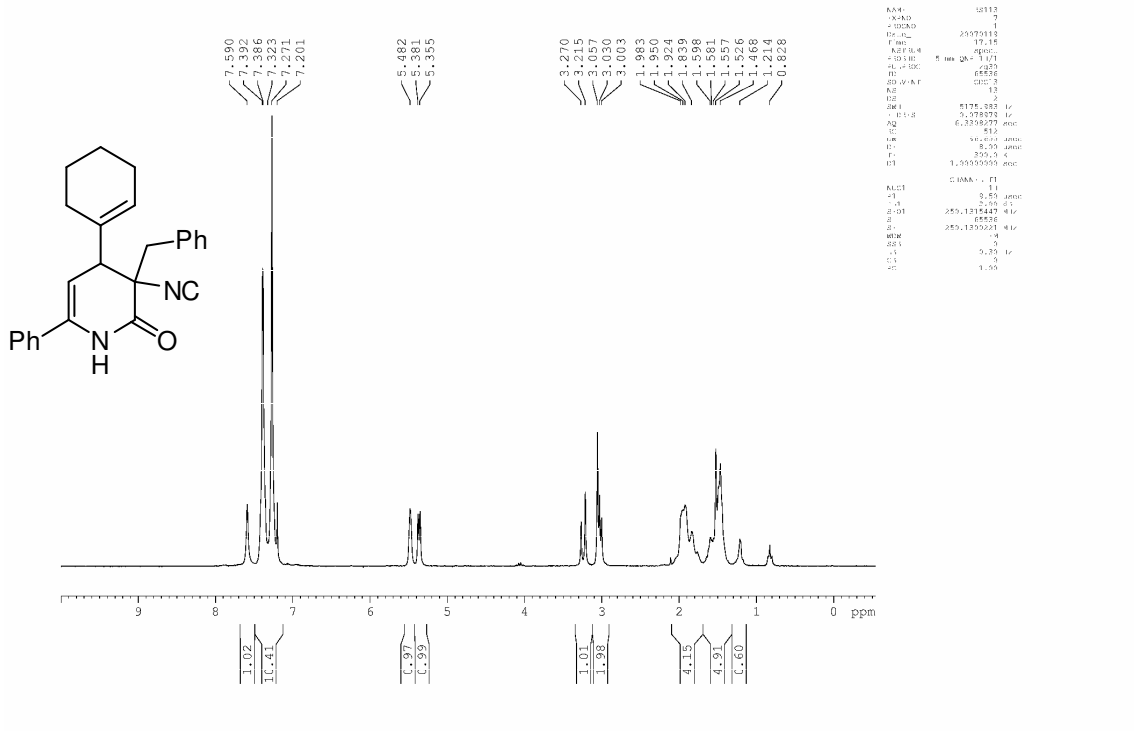
3,4-Dihydropyridin-2-one (**12w**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



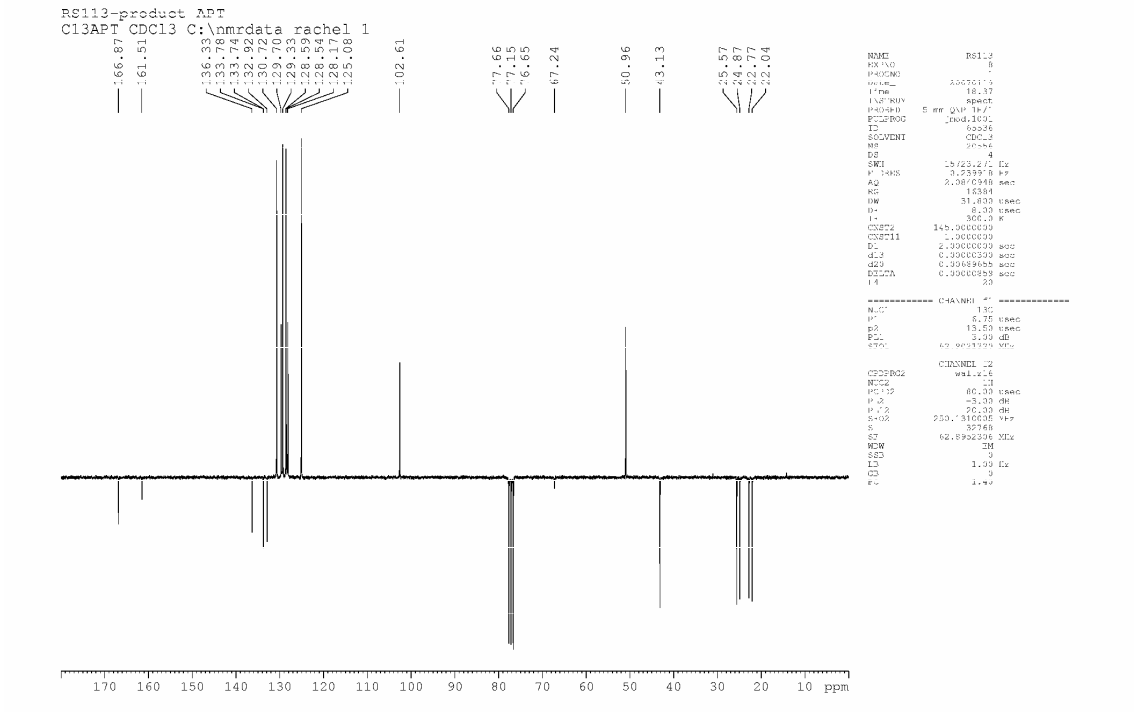
^{13}C{1H} NMR (62.90 MHz, $CDCl_3$)



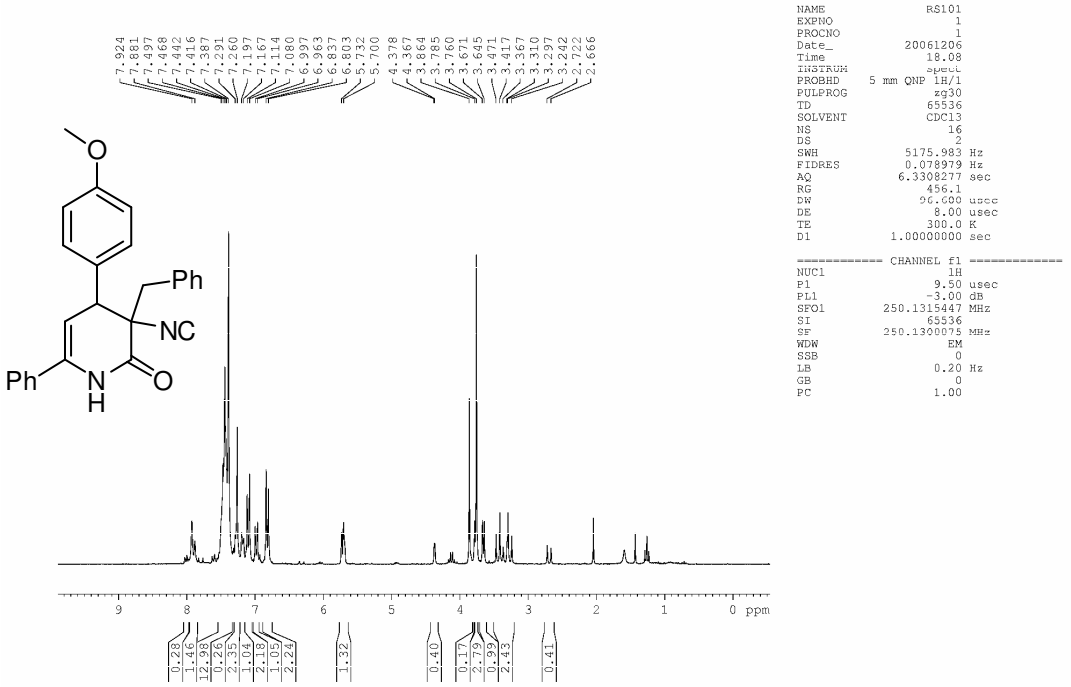
3,4-Dihydropyridin-2-one (**12x**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



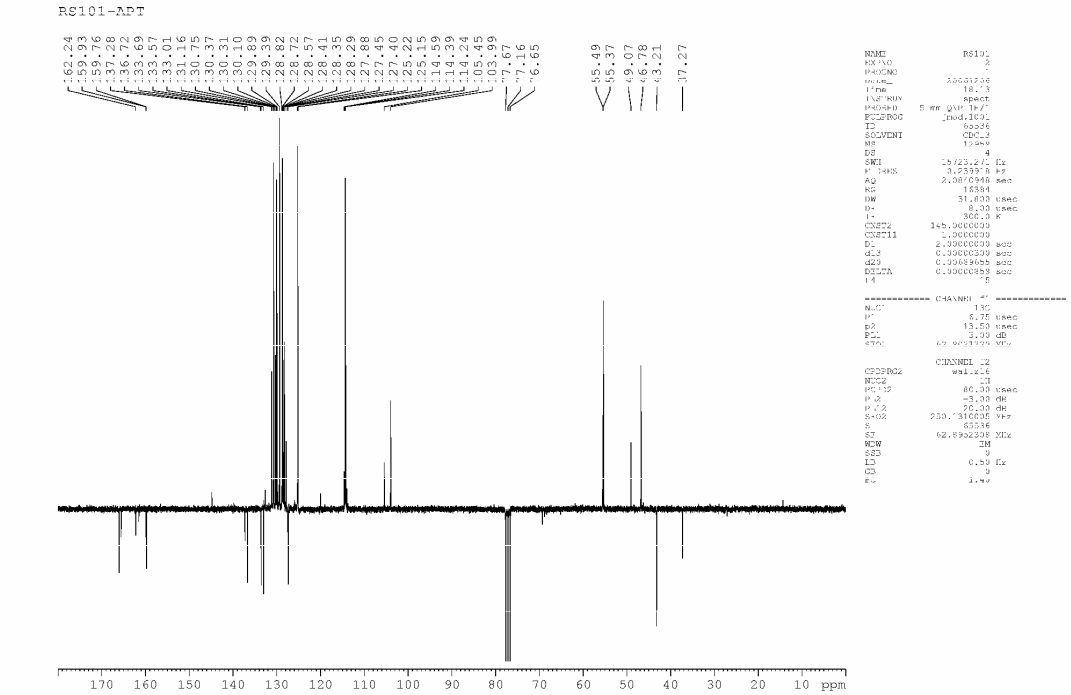
^{13}C{1H} NMR (62.90 MHz, $CDCl_3$)



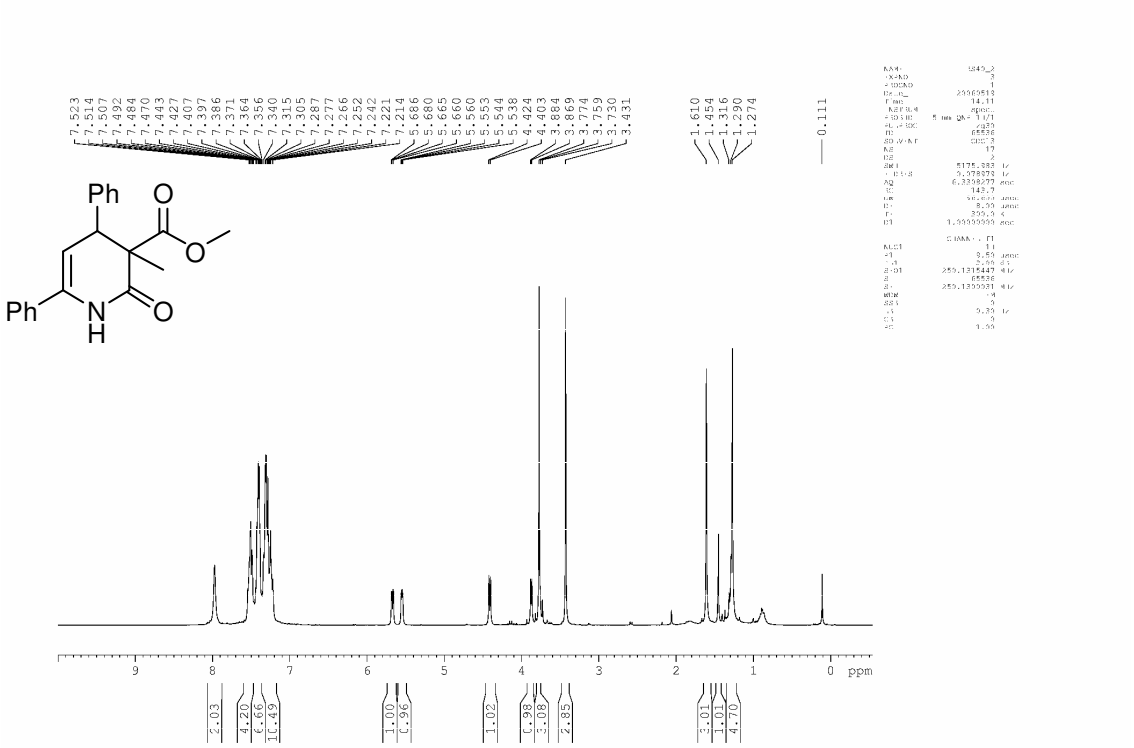
3,4-Dihydropyridin-2-one (**12y**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



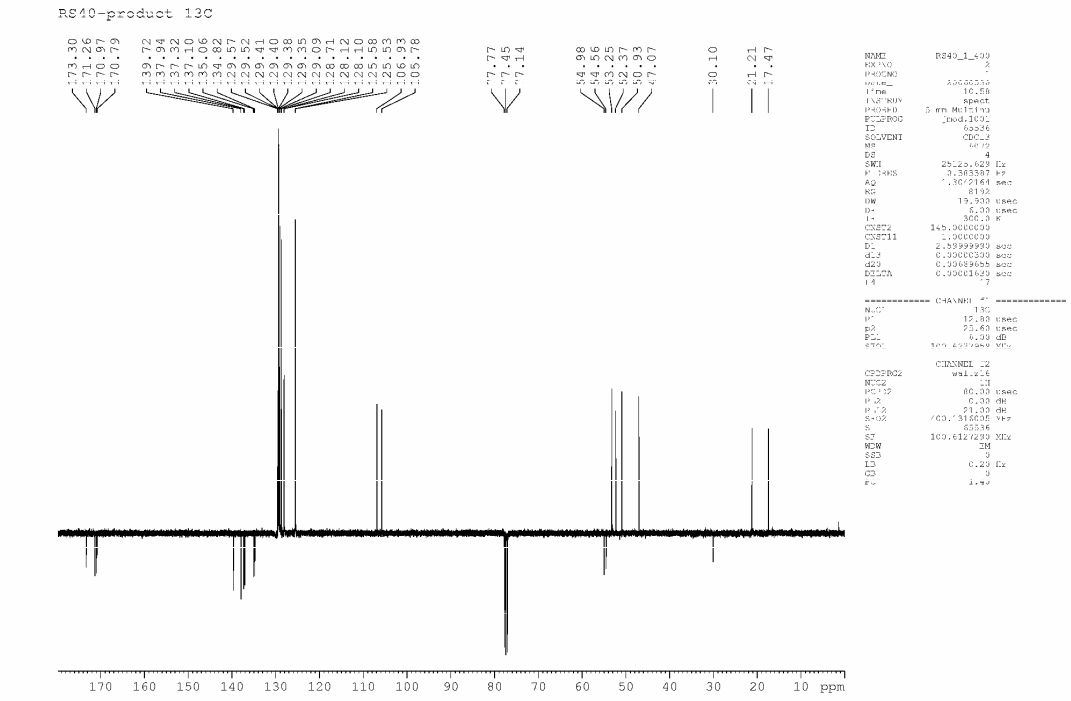
^{13}C{1H} NMR (62.90 MHz, $CDCl_3$)



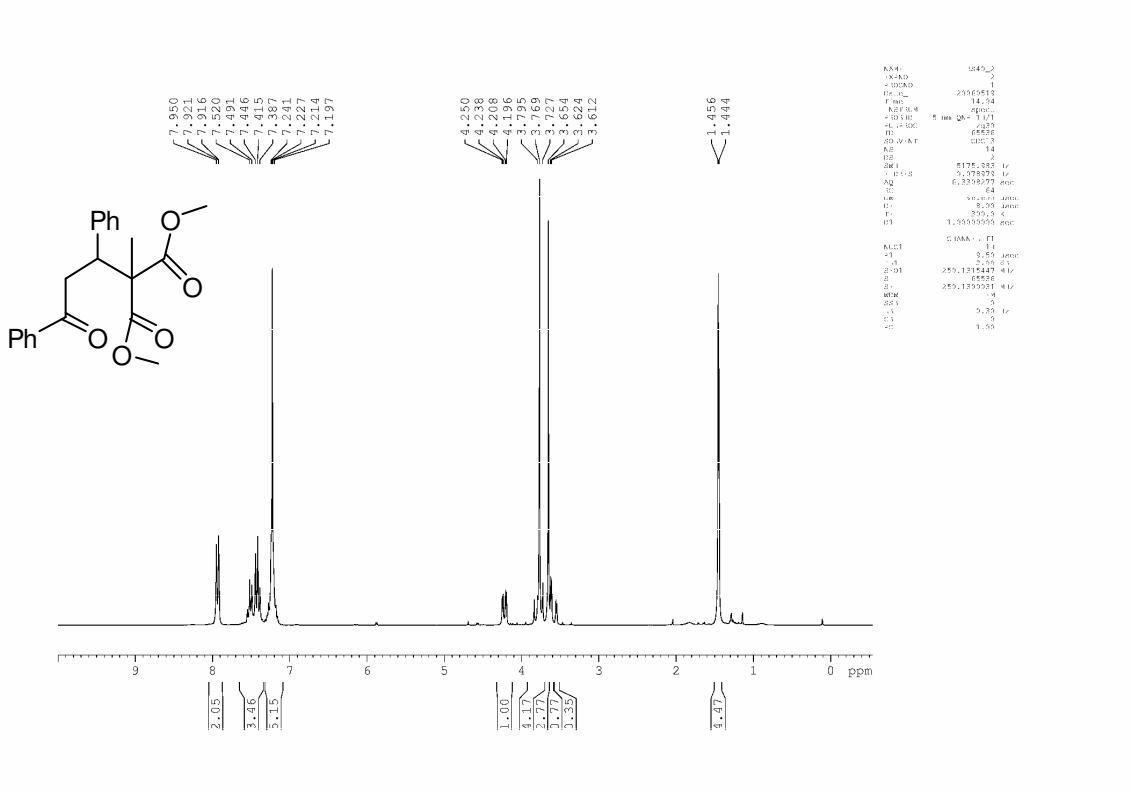
3,4-Dihydropyridin-2-one (**35a**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



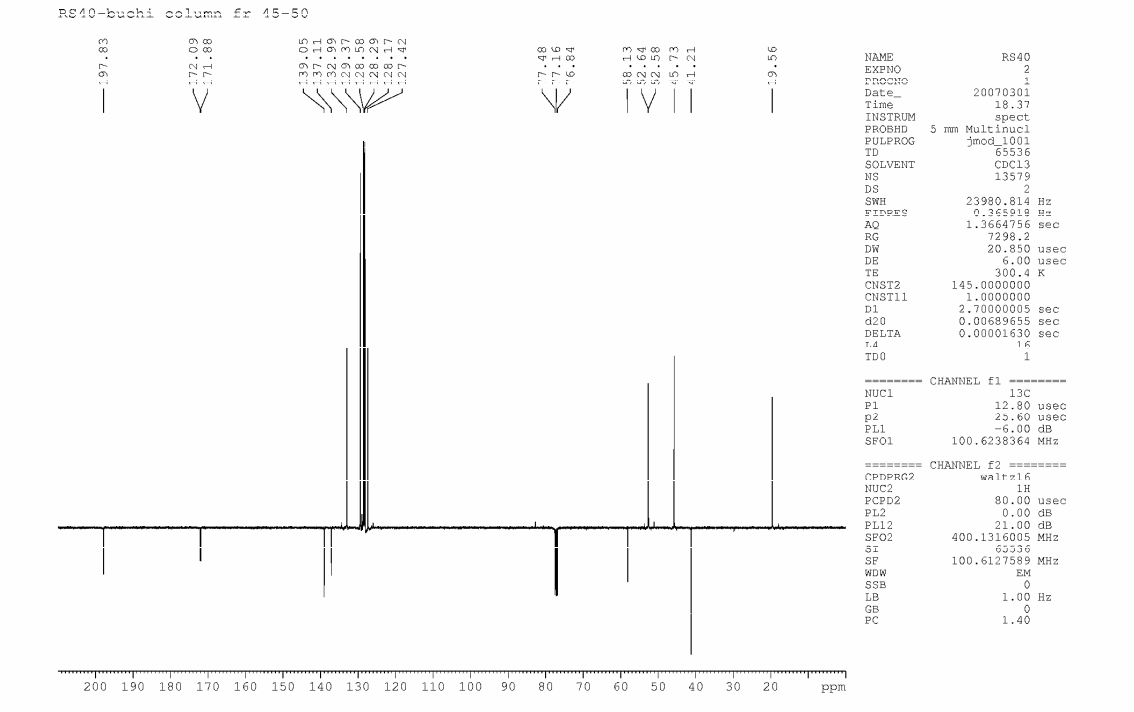
^{13}C{1H} NMR (100.62 MHz, $CDCl_3$)



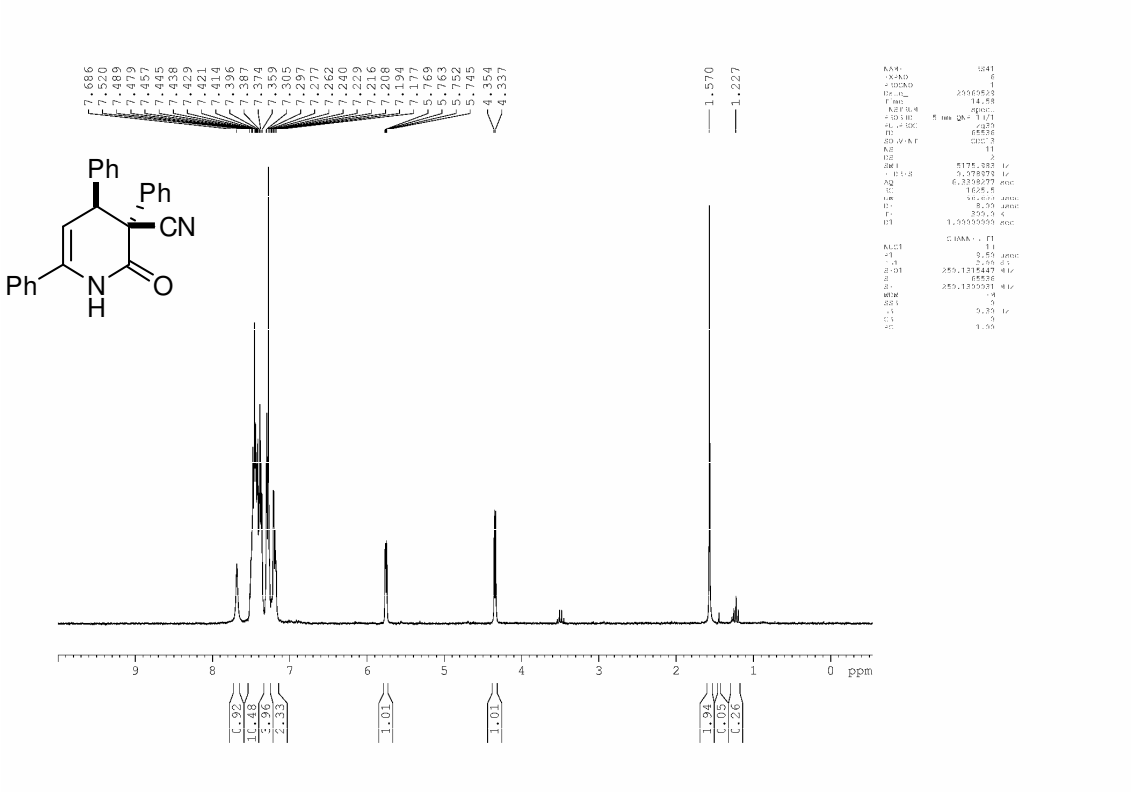
Ketone (**38**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



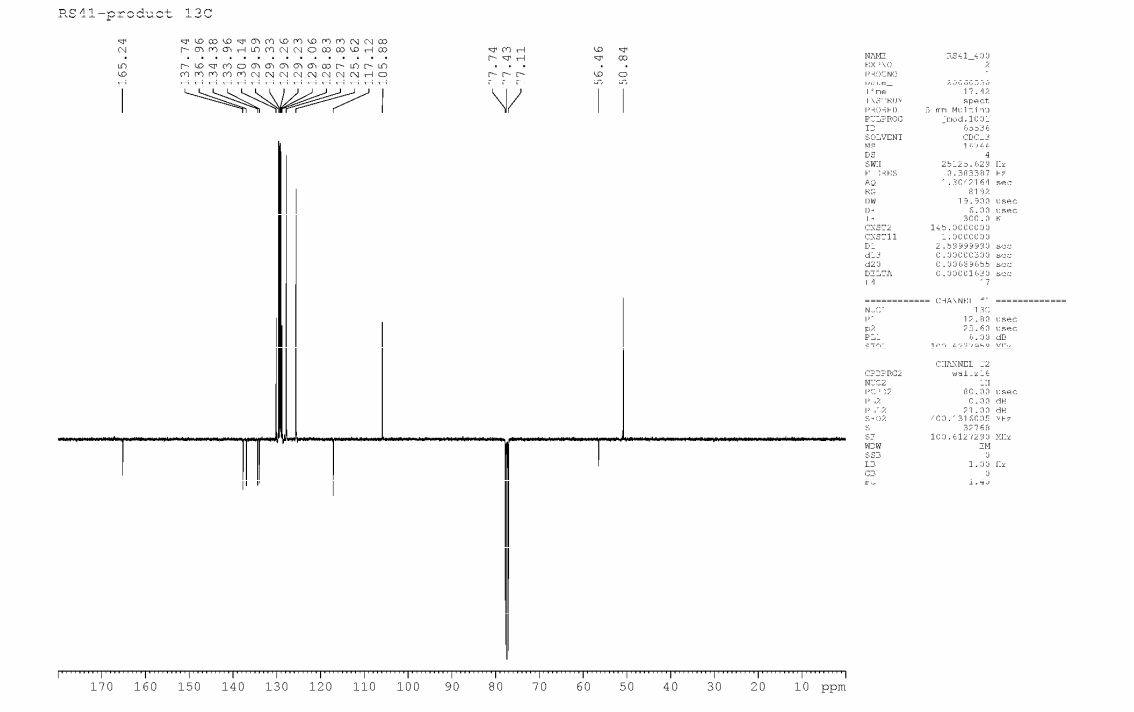
^{13}C{1H} NMR (100.62 MHz, $CDCl_3$)



3,4-Dihydropyridin-2-one (**35b**): ^{1}H NMR (250.13 MHz, $CDCl_3$)



^{13}C{1H} NMR (100.62 MHz, $CDCl_3$)



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[2] Major and minor peaks in the ^{1}H-NMR and ^{13}C-NMR are denoted where possible.

[3] A second chromatographic purification step afforded the product (*c*hexane: EtOAc 8:2) completely pure, however some of the *trans*-diastereomer is lost.

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[8] The presence of the *trans*-diastereomer is neclectable, therefore only the spectrum of the *cis*-diastereomer is given.

[9] Trace amounts of the *trans*-diastereomer were detected in the 1H NMR of the crude product, however this could not be isolated as a pure compound.

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