Supporting Information

A greener procedure for the synthesis of α-ureidophosphonates under ultrasound irradiation. X-ray crystallographic study

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1. General data

All chemicals and solvents were purchased from common commercial sources and were used as received without any further purification. All reactions were monitored by TLC on silica Merck 60 F_{254} percolated aluminum plates and were developed by spraying with ninhydrin solution. Column chromatography was performed with Merck silica gel (230-400 mesh). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Brücker or Jeol spectrometer at 250, or 400 MHz. Chemical shifts is reported in δ units (ppm) with TMS as reference (δ 0.00). All coupling constants (*J*) are reported in Hertz. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Brücker or Jeol at 60, 75 or 100 MHz. Chemical shifts are reported in δ units (ppm) relative to $CDCl_3$ (δ 77.0). Phosphorus nuclear magnetic resonance (^{31}P NMR) spectra were recorded on a Brücker or Jeol at 75, 100 or 161 MHz. Infrared spectra were recorded on a Perkin Elmer 600 spectrometer. Elemental analysis was recorded on a EURO E.A 3700. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes. Ultrasound assisted reactions were carried out using a FUNGILAB ultrasonic bath with a frequency of 40 kHz and a nominal power of 250 W. The reactions were carried out in an open glass tube (diameter: 25 mm; thickness: 1 mm; volume: 20 mL) at 75°.

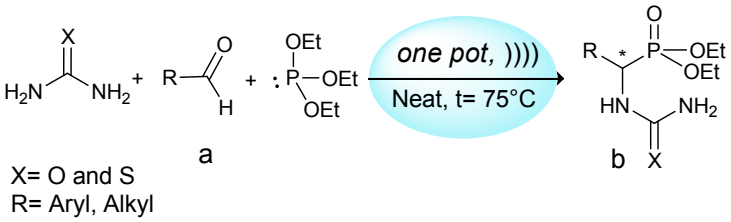
2. Crystallography

A single crystal of the studied compound, 13b, $C_{15}H_{24}N_2O_4P$, with dimensions of 0.06×0.11× 0.13 mm^3, was selected for single crystal X-ray diffraction analysis. Data collection was performed, at 295(2)K, on a Bruker APEX II diffractometer, CCD area detector equipped with a graphite monochromatizedMoKα radiation (λ= 0.71073Å).***Crystallographic data*** for 13b: $C_{15}H_{24}N_2O_4P$, M = 327.33, T = 295(2) K, monoclinic, space group P21/n (no. 14), a = 9.6789(5), b = 9.1089(4), c = 20.6717(9)Å , β=93.303(2)°, V = 1819.48(15) Å3, Z = 4, Dc =

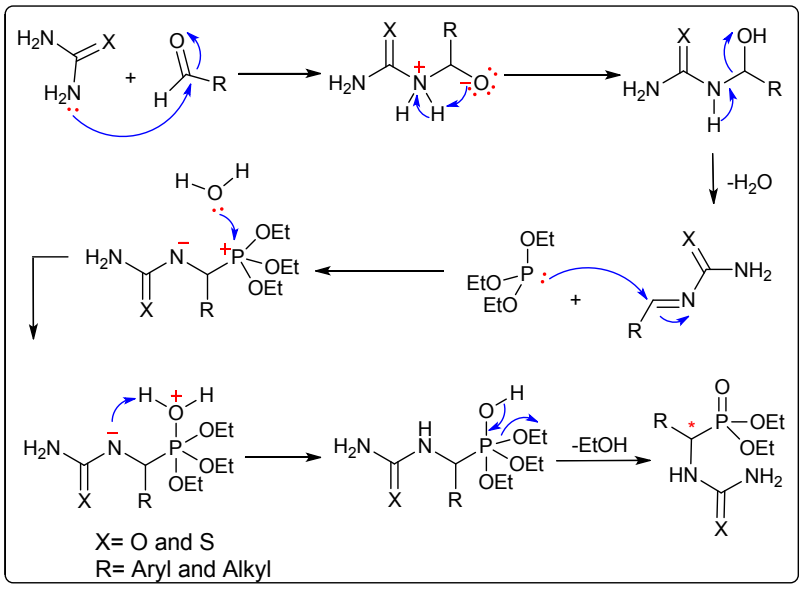
1.195 Mg m−3, μ= 0.169 mm−1, independent reflections = 3602 [Rint = 0.0379], R1 [for 2291 reflections with I > 2r(I)] = 0.0675, wR2 (all data = 0.1907).

3. Typical experimental procedure for the synthesis of α- ureidophosphonates

In a glass tube (diameter: 25 mm; thickness: 1 mm; volume: 20 mL taken a mixture of aldehyde (1 mmol) and urea (1 mmol) at 75^0 C, (1 mmol) triethylphosphite was added. The reaction mixture was subjected to the ultrasonicationwith a frequency of 40 kHz for appropriate time. After completion of the reaction, as indicated by TLC, silica gel; dichloromethane:methanol (9:1), a (6:4) mixture of diethyl ether and n-hexane was added to the reaction mixture and pure product was crystallized to 6° C overnight. The product was finally filtered and dried.

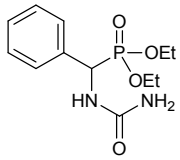


Scheme 1 Synthesis of α-ureidophosphonatesunder ultrasound irradiation.



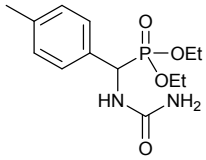
Scheme2 Mechanistic proposal for the synthesis of α-ureidophosphonates.

4. Spectral data



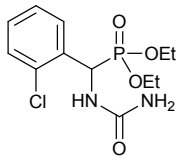
Diethyl [α-ureido-(phenyl)]methylphosphonate (Table 2, Entry 1b)

White solid. Yield 85 %. M.p. 197-199 °C.R_f = 0.41 (CH_2Cl_2/MeOH:95/05). ν_{max}(KBr/cm^{-1}) 3433.35, 3315.6, 3224.56, 1686.37, 1235.85, 1023.δ_P(120 MHz, $CDCl_3$) 21.61 ppm.δ_H(400 MHz, $CDCl_3$) 1.032 (t, *J* 7.20 Hz, 3H, CH_3-CH_2O), 1.29 (t, *J* 6.89 Hz, 3H, CH_3-CH_2O), 3.60-3.64 (m, 1H, CH_2-O), 3.85-3.89 (m, 1H, CH_2-O), 4.06-4.17 (m, 2H, CH_2-O), 5.14 (s, 2H, NH), 5.17-5.21 (dd, J_1 8.00, J_2 17.45 Hz, 1H, CH*), 7.12-7.23 (m, 5H, H-Ar), 7.26 (s,1H, NH) ppm.δ_C (100 MHz, $CDCl_3$) 16.32, 16.59, 54.05, 63.96, 64.11, 124.46, 126.31, 126.36, 126.75, 126.9, 134.24, 159.05 ppm.Ms (m/z): 287 (M+1). Anal. Calc. for $C_{12}H_{19}N_2O_4P$: C, 50.35; H, 6.69; N, 9.79.Found: C, 50.30; H, 6.73; N, 9.85.



Diethyl [α-ureido-(4-methylphenyl)]methyl phosphonate (Table 2, Entry 2b)

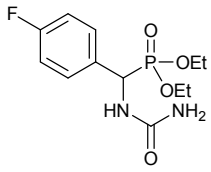
White solid. Yield 78 %. M.p. 184-186 °C.R_f = 0.43 (CH_2Cl_2/MeOH:95/05). ν_{max}(KBr/cm^{-1}) 3433.33, 3315.93, 3264.5, 1666.37, 1235.85.δ_P(120 MHz, $CDCl_3$) 20.61 ppm.δ_H (250 MHz, $CDCl_3$) 1.08 (t, *J* 7.12 Hz, 3H, CH_3-CH_2O), 1.32 (t, *J* 6.94 Hz, 3H, CH_3-CH_2O), 2.38 (s, 3H, CH_3-CAr), 3.68-3.72 (m, 1H, CH_2-O), 3.81-3.85 (m, 1H, CH_2-O), 4.27-4.32 (m, 2H, CH_2-O), 5.25 (s, 2H, NH), 5.31-5.45 (dd, J_1 9.80, J_2 21.66 Hz, 1H, CH*), 7.10-7.4 (m, 4H, H-Ar), 7.56 (s, 1H, NH) ppm.δ_C (100 MHz, $CDCl_3$) 16.68, 16.87, 24.2, 53.5, 63.45, 64.54, 124.7, 126.2, 132.4, 135.45, 135.95, 136.1, 160.4 ppm. Ms (m/z): 301.2 (M+1). Anal. Calc. for $C_{13}H_{21}N_2O_4P$: C, 52.00; H, 7.05; N, 9.33.Found: C, 52.05; H, 7.09; N, 9.37.



Diethyl [α-ureido-(2-chlorophenyl)]methylphosphonate (Table 2, Entry 3b)

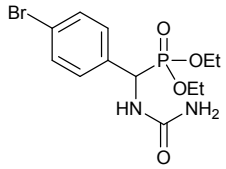
Color solid.Yield 83 %. M.p. 202-204 °C.R_f = 0.42 (CH_2Cl_2/MeOH:95/05).ν_{max} (KBr/cm-1)·3424.31, 3323.21, 3203.28 1687.51, 1220.90.δ_P(120 MHz, $CDCl_3$) 22.24 ppm.δ_H (400 MHz, $CDCl_3$) 1.04 (t, *J* 7.20 Hz, 3H, CH_3-CH_2O), 1.36 (t, *J* 7.20 Hz, 3H, CH_3-CH_2O), 3.70-3.75 (m, 1H, CH_2-O), 3.80-3.90 (m, 1H, CH_2-O), 4.20-4.30 (m, 2H, CH_2-O), 5.21 (s, 2H, NH), 5.59 (dd, J_1=9.60, J_2 22.00 Hz, 1H, CH*), 7.31-7.54 (m, 4H, H-Ar), 7.60 (s, 1H, NH)

ppm.δ_C(100 MHz, $CDCl_3$) 16.12, 16.51, 46.79, 48.15, 63.76, 64.01, 127.22, 129.22, 129.55, 133.97, 134.05, 134.58, 158.32 ppm.Ms (m/z): 321.1 (M+1). Anal. Calc. for $C_{12}H_{18}ClN_2O_4P$: C, 44.94; H, 5.66; N, 11.05.Found: C, 45.02; H, 5.61; N, 11.01.



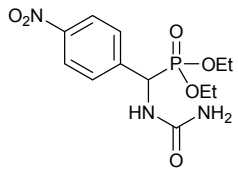
Diethyl [α-ureido-(4-fluorophenyl)]methylphosphonate (Table 2, Entry 5b)

White solid. Yield 81 %.M.p. 198-200 °C.R_f = 0.40 (CH_2Cl_2/MeOH:95/05). ν_{max} (KBr/cm-[1])3447.46, 3330.45, 3259.60, 1689.16, 1238.12.δ_P(100 MHz, $CDCl_3$) 23.12 ppm.δ_H (250 MHz, $CDCl_3$) 1.04 (t, *J* 7.11 Hz, 3H, CH_3-CH_2O), 1.38 (t, *J* 6.92 Hz, 3H, CH_3-CH_2O), 3.67-3.70 (m, 1H, CH_2-O), 3.87-3.90 (m, 1H, CH_2-O), 4.21-4.25 (m, 2H, CH_2-O), 5.19 (s, 2H, NH), 5.31-5.48 (dd, J_1 9.96, J_2 21.81, Hz, 1H, CH*), 7.21-7.48 (m, 4H, H-Ar), 7.54 (s, 1H, NH) ppm.δ_C (100 MHz, $CDCl_3$) 16.18, 16.47, 54.26, 64.02, 64.13, 126.24, 126.76, 130.27, 130.36, 134.00, 136.50, 161.06 ppm.Ms (m/z): 305 (M+1). Anal. Calc. for $C_{12}H_{18}FN_2O_4P$: C, 47.37; H, 5.96; N, 9.21.Found: C, 47.29; H, 5.92; N, 9.26.



Diethyl [α-ureido-(4-bromophenyl)]methylphosphonate(Table 2, Entry 7b)

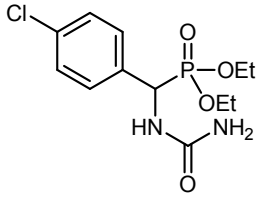
White solid. Yield 79 %.M.p. 188-190 °C.R_f = 0.40 (CH_2Cl_2/MeOH:95/05). ν_{max} (KBr/cm-[1]) 3446.50, 3218.4, 3213.02, 1660.49, 1559.08, 1238.02.δ_C(120 MHz, $CDCl_3$) 21.23 ppm.δ_H (250 MHz, $CDCl_3$) 1.14 (t, *J* 6.94 Hz, 3H, CH_3-CH_2O), 1.41 (t, *J* 6.87 Hz, 3H, CH_3-CH_2O), 3.76-3.81 (m, 1H, CH_2-O), 3.88-3.92 (m, 1H, CH_2-O), 3.99-4.27 (m, 2H, CH_2-O), 5.21 (s, 2H, NH), 5.25-5.48 (dd, J_1 9.89, J_2 22.03 Hz, 1H, CH*), 7.21-7.52 (m, 4H, H-Ar), 7.6 (s, 1H, NH) ppm.δ_C (75 MHz, $CDCl_3$) 16.20, 16.42, 53.80, 63.85, 64.08, 124.7, 126.2, 127.05, 128.12, 132.4, 137.45, 160.04 ppm. Ms (m/z): 366 (M+1). Anal. Calc. for $C_{12}H_{18}BrN_2O_4P$: C, 39.56; H, 4.94; N, 7.69.Found: C, 39.48; H, 4.88; N, 7.57.



Diethyl [α-ureido-(4-nitrophenyl)]methylphosphonate (Table 2, Entry 8b)

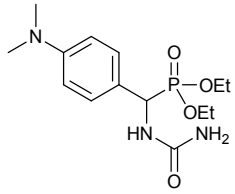
White solid. Yield 85 %.M.p. 203-205 °C.R_f = 0.45 (CH_2Cl_2/MeOH:95/05). ν_{max} (KBr/cm-[1])3433.35, 3315.6, 3224.56, 1666, 1242, 1023 cm. δ_P(120 MHz, $CDCl_3$) 21.57 ppm.δ_H (400 MHz, $CDCl_3$) 1.03 (t, *J* 7.20 Hz, 3H, CH_3-CH_2O), 1.31 (t, *J* 6.89 Hz, 3H, CH_3-CH_2O), 3.60-

3.64 (m, 1H, CH_2-O), 3.85-3.91 (m, 1H, CH_2-O), 4.11-4.17 (m, 2H, CH_2-O), 5.14 (s, 2H, NH), 5.17-5.21 (dd, J_1 9.25, J_2 21.75 Hz, 1H, CH*), 7.12-7.23 (m, 5H, H-Ar), 7.26 (s,1H, NH) ppm.δ_C (100 MHz, $CDCl_3$) 16.32, 16.41, 55.42, 63.14, 63.33, 127.06, 126.31, 126.36, 128.55, 136.58, 136.58, 161.68 ppm.Ms (m/z): 332 (M+1). Anal. Calc. for $C_{12}H_{19}N_2O_4P$: C, 50.35; H, 6.69; N, 9.79.Found: C, 50.21; H, 6.73; N, 9.78.



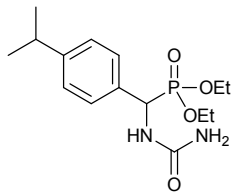
Diethyl [α-ureido-(4-chlorophenyl)]methyl phosphonate (Table 2, Entry 8b)

White solid.Yield 80 %.M.p. 201-203 °C.R_f = 0.42 (CH_2Cl_2/MeOH:95/05). ν_{max} (KBr/cm-[1])3436.17, 3321.12, 3262.15, 1689.49, 1239.69.δ_P(120 MHz, $CDCl_3$) 21.82 ppm.δ_H(400 MHz, $CDCl_3$) 1.10 (t, *J* 7.03 Hz, 3H, CH_3-CH_2O), 1.34 (t, *J* 7.06 Hz, 3H, CH_3-CH_2O), 3.69-3.73 (m, 1H, CH_2-O), 3.85-3.99 (m, 1H, CH_2-O), 4.08-4.15 (m, 2H, CH_2-O), 5.26 (s, 2H, NH), 5.31-5.36 (dd, J_1 9.40, J_2 20.10 Hz, 1H, CH*), 7.25-7.34 (m, 4H, H-Ar), 7.55 (s, 1H, NH) ppm.δ_C (100 MHz, $CDCl_3$) 16.24, 16.51, 53.14, 53.91, 63.59, 63.89, 128.77, 129.42, 129.48, 134.70, 158.58 ppm.Ms (m/z); 321 (M+1). Anal. Calc. for $C_{12}H_{18}ClN_2O_4P$: C, 44.94; H, 5.66; N, 11.05.Found: C, 45.02; H, 5.61; N, 11.01.



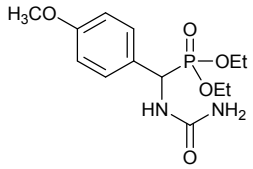
Diethyl [α-ureido-(4-dimethylaminophenyl)]methylphosphonate(Table 2, Entry 11b)

Yellow solid. Yield 85%.M.p. 192-194 °C. R_f = 0.47 (CH_2Cl_2/MeOH:95/05). ν_{max} (KBr/cm-[1]) 3424.31, 3323.21, 3203.26, 1687.51, 1220.90, 1017.76.δ_P($CDCl_3$) 21.85.δ_H($CDCl_3$, 400 MHz) 1.13 (t, 3H, *J* 7.22 Hz, CH_3-CH_2O), 1.39 (t, 3H, *J* 7.12 Hz, CH_3-CH_2O), 2.93 (s, 6H, $2CH_3$-N), 3.74-3.83 (m, 1H, CH_2-O), 3.88-3.97 (m, 1H, CH_2-O), 4.15-4.30 (m, 2H, CH_2-O), 5.18 (s, 2H, NH), 5.32 (dd, 1H, J_1 9.96, J_2 21.11 Hz, CH*), 7.34-7.45 (m, 4H, H-Ar), 7.50 (s, 1H, NH). δ_C ($CDCl_3$, 100.6 MHz) 16.30, 16.35, 54.5, 54.57, 64.05, 64.10, 127.75, 127.81, 127.94, 135.12, 135.45, 137.60, 159.25 ppm.Ms (m/z): 329.7 (M+1); Anal. Calc. for $C_{14}H_{24}N_3O_4P$. C, 51.06; H, 7.35; N, 12.76. Found: C, 51.11; H, 7.37, N, 12.75.



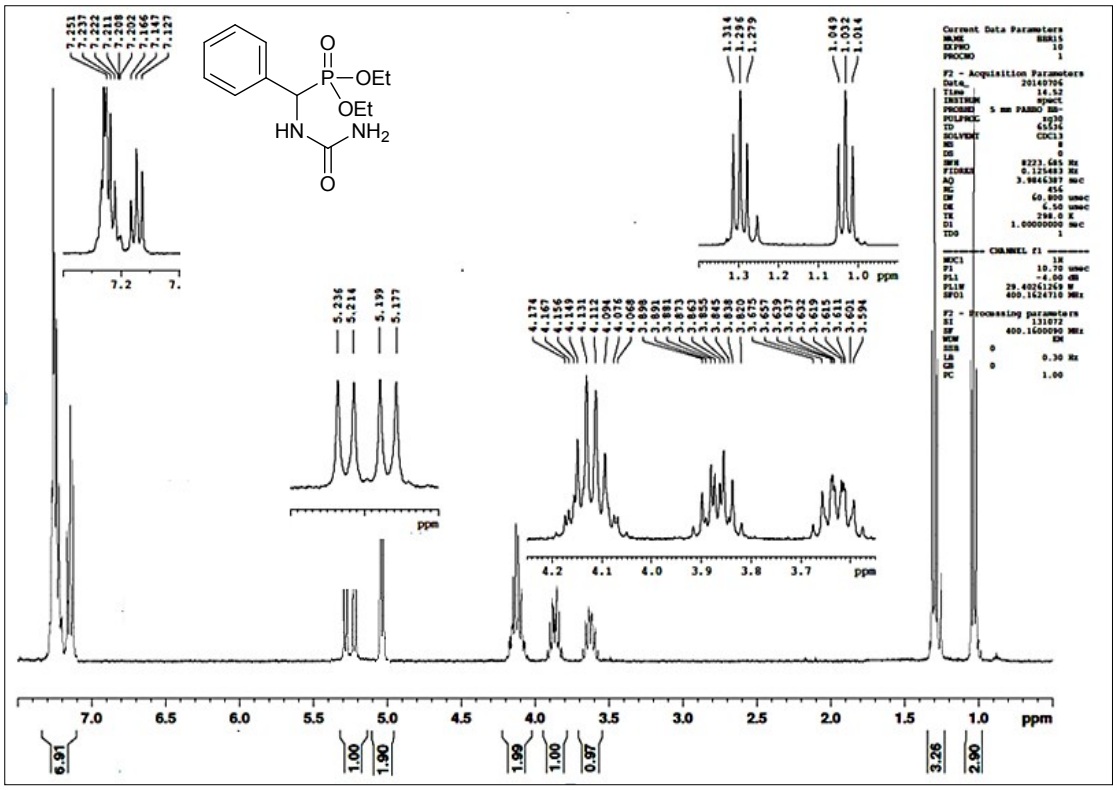
Diethyl [α-ureido-(4-isopropylphenyl)]methylphosphonate(Table 2, Entry 13b)

Cristal.Yield 85%. M.p.197-199 °C.R_f = 0.46 (CH_2Cl_2/MeOH:95/05). ν_{max}(KBr/cm^{-1}) 3443.17, 3362.23, 3252.64, 1664, 1238.02, 1028.42.δ_P($CDCl_3$) 21.48.δ_H ($CDCl_3$, 250 MHz) 1.09 (2d, 6H, *J* 7.05 Hz, $2CH_3$-CH), 1.11 (t, 3H, *J* 7.04 Hz, CH_3-CH_2O), 1.31 (t, 3H, *J* 7.11 Hz, CH_3-CH_2O), 2.89 (m, 1H, CH-Ar), 3.71-3.79 (m, 1H, CH_2-O), 3.84-3.91 (m, 1H, CH_2-O), 4.11-4.24 (m, 2H, CH_2-O), 5.18 (s, 2H, NH), 5.32 (dd, 1H, J_1 9.91, J_2 19.75 Hz, CH), 7.19-7.49 (m, 4H, H-Ar), 7.51 (s, 1H, NH).δ_C ($CDCl_3$, 100.6 MHz) 16.8, 16.9, 21.15, 23.14, 34.5, 53.4, 63.5, 64.5, 124.12, 124.56, 127.8, 131.2, 132.3, 139.1, 160.1 ppm.Ms (m/z): 328.7 (M^+). Anal. Calcd for $C_{15}H_{25}N_2O_4P$. C, 54.87; H, 7.67; N, 5.53. Found: C, 54.81; H, 7.70; N, 5.56

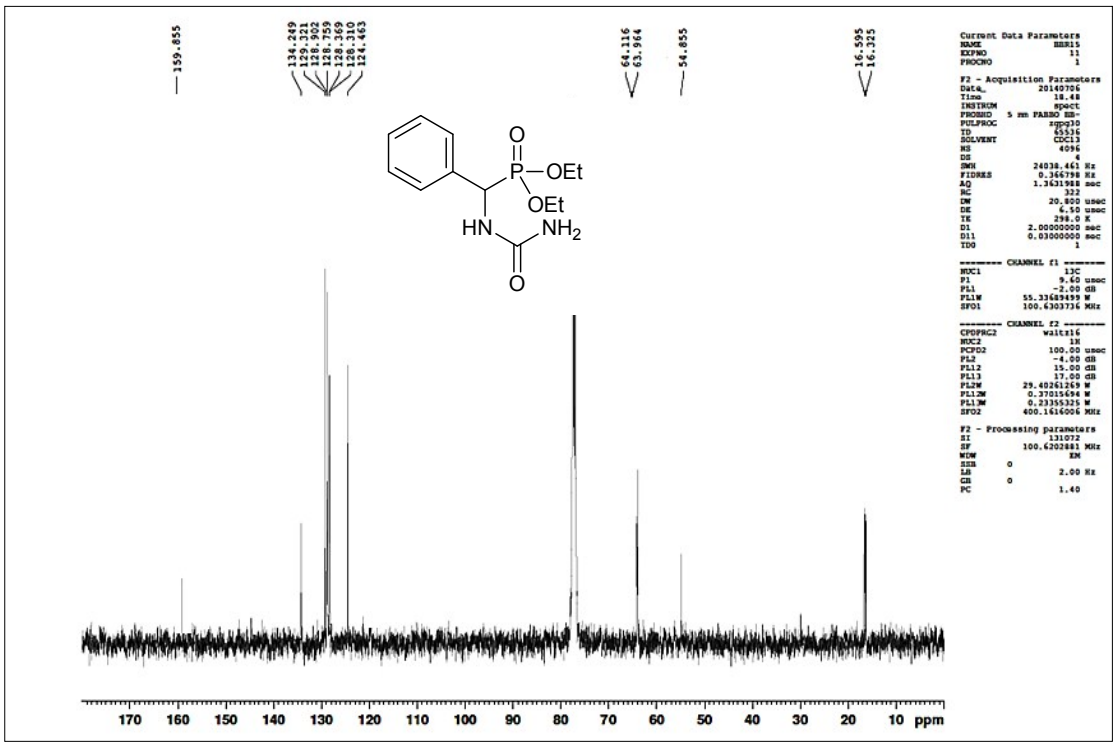


Diethyl [α-ureido-(4-methoxyphenyl)] methyl phosphonate(Table 2, Entry 15b)

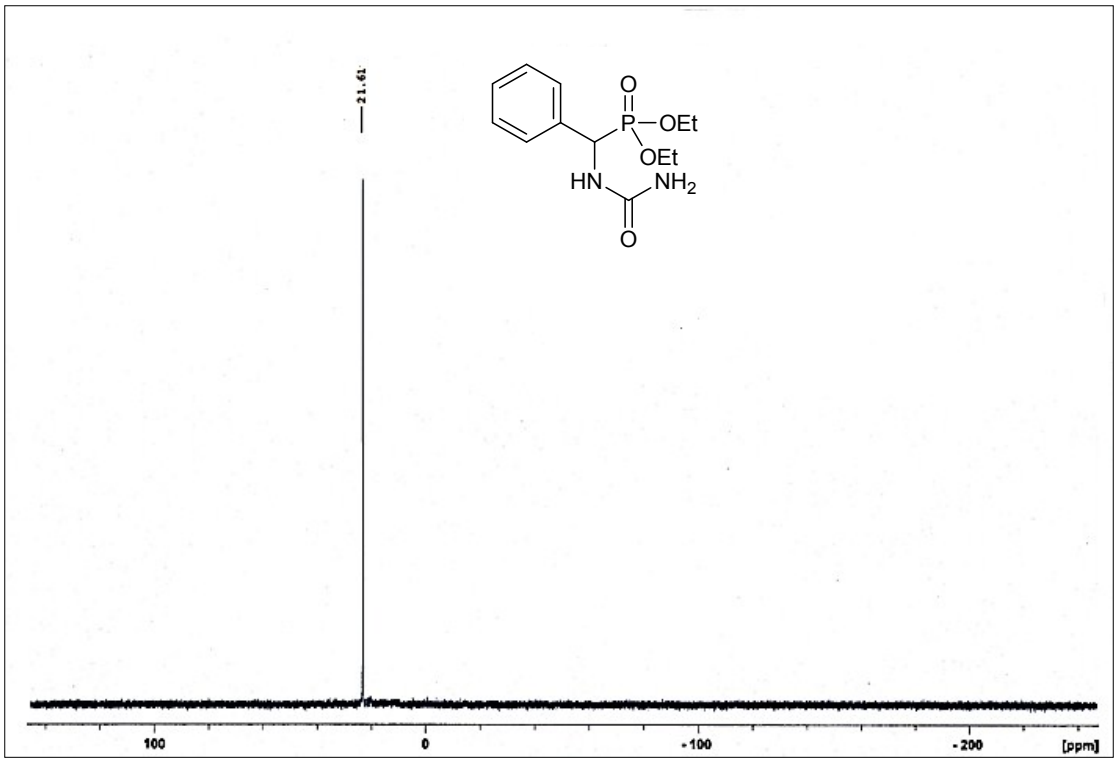
Wide solid. Yield 78 %.M.p. 204-206 °C.R_f = 0.46 (CH_2Cl_2/MeOH:95/05). ν_{max}(KBr/cm^{-1})3446.58, 3314.26, 3213.02, 1660.49, 1238.02, 1084.15.δ_P(120 MHz, $CDCl_3$) 21.15 ppm.δ_H (250 MHz, $CDCl_3$) 1.18 (t, *J* 7.20 Hz, 3H, CH_3-CH_2O), 1.35 (t, *J* 7.00 Hz, 3H, CH_3-CH_2O), 3.76-3.86 (m, 1H, CH_2-O), 3.91-3.96 (m, 1H, CH_2-O), 3.97-4.10 (m, 2H, CH_2-O), 5.14 (s, 2H, NH2), 5.28 (dd, J_1 9.21, J_2 22.40 Hz, 1H, CH*), 7.10 (dd, *J* 9.6 Hz, 1H, NH), 7.31 (d, *J* 8.2 Hz, 2H, H-Ar), 7.52 (d, *J* 8.2 Hz, 2H, H-Ar) ppm.δ_C (100 MHz, $CDCl_3$) 16.7, 16.9, 52.5, 53.4 ,63.9, 64.7, 123.6, 129.7, 129.9, 131.8, 131.8, 136.5, 159.95 ppm. Ms (m/z): 317.1 (M+1). Anal. Calc. for $C_{13}H_{21}N_2O_5P$: C, 49.37; H, 6.69; N, 8.86.Found: C, 49.41; H, 6.67; N, 8.84.



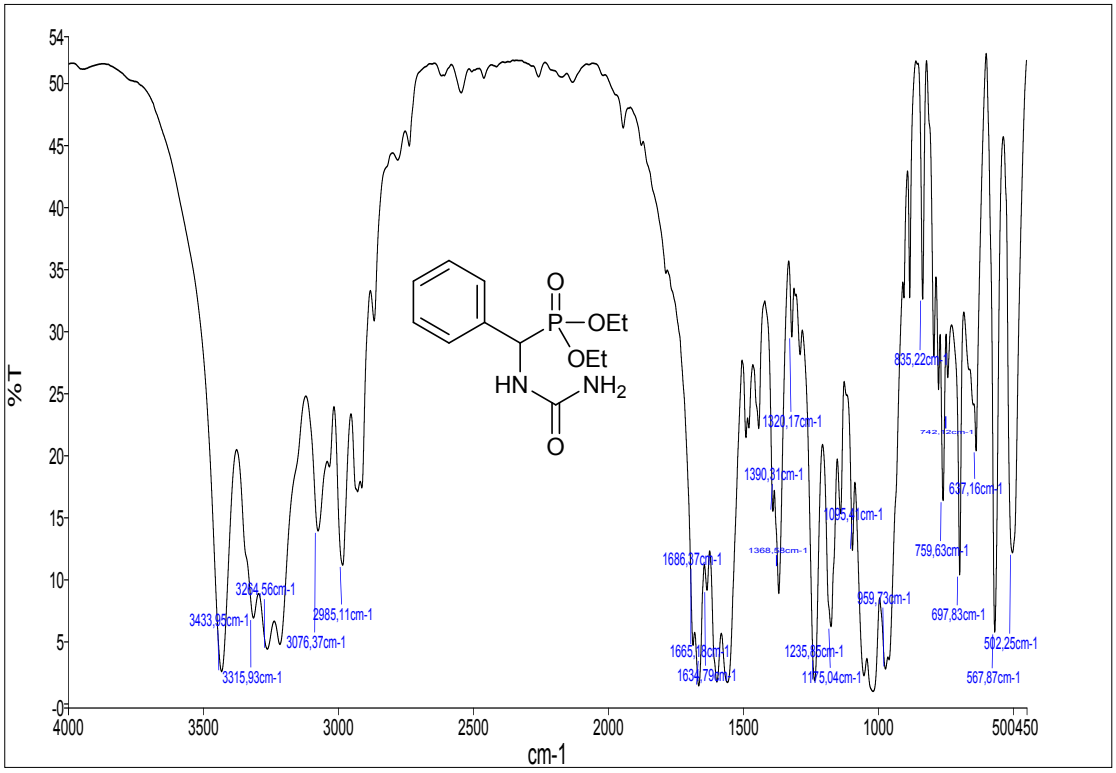
^{1}H NMR spectrum: Diethyl [α-ureido-(phenyl)]methyl phosphonate



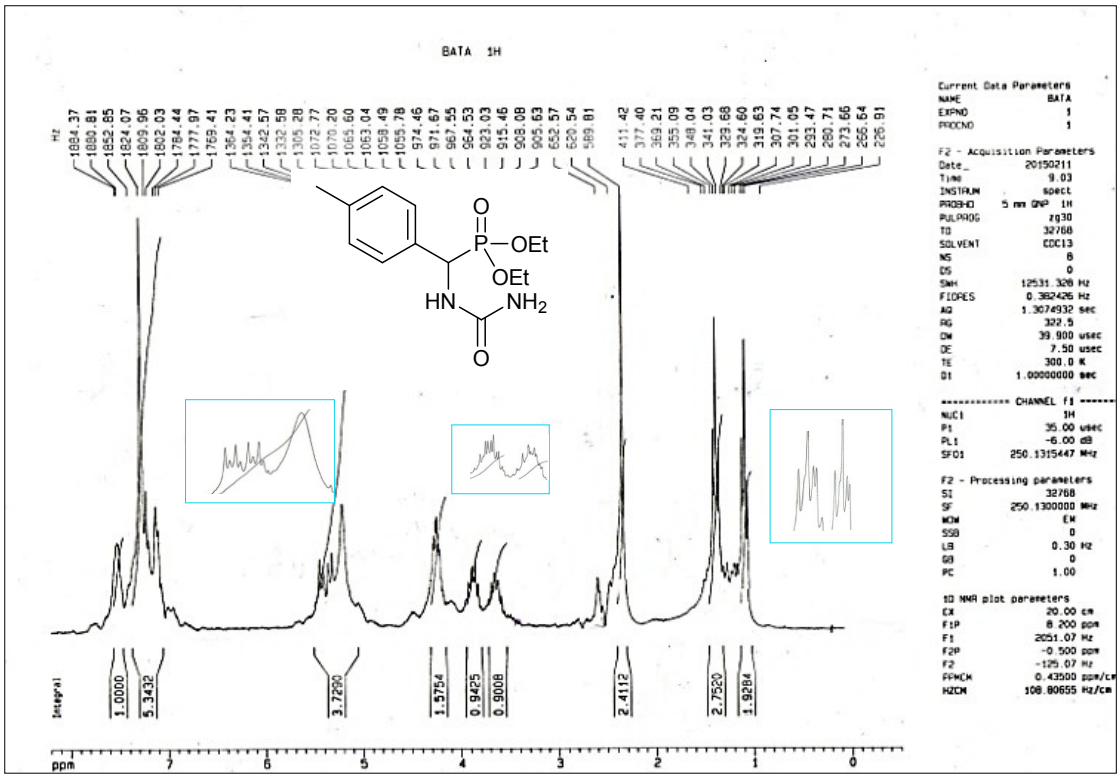
^{13}C NMR spectrum: Diethyl [α-ureido-(phenyl)]methyl phosphonate



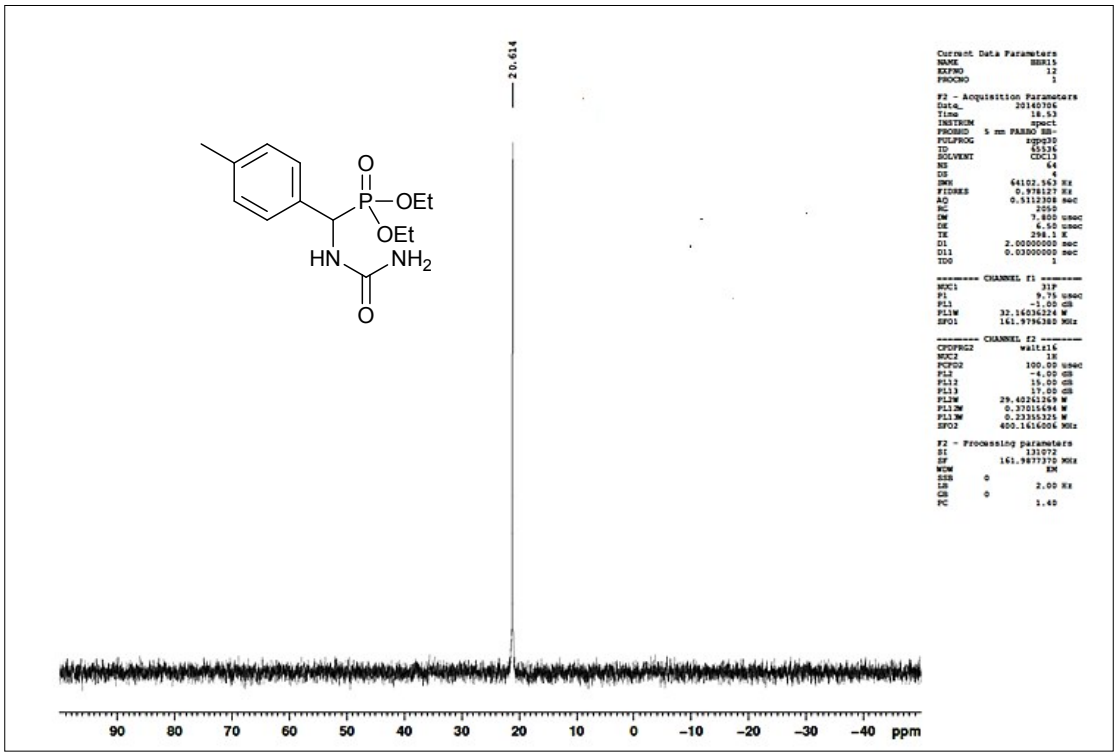
^{31}P NMR spectrum: Diethyl [α-ureido-(phenyl)]methyl phosphonate



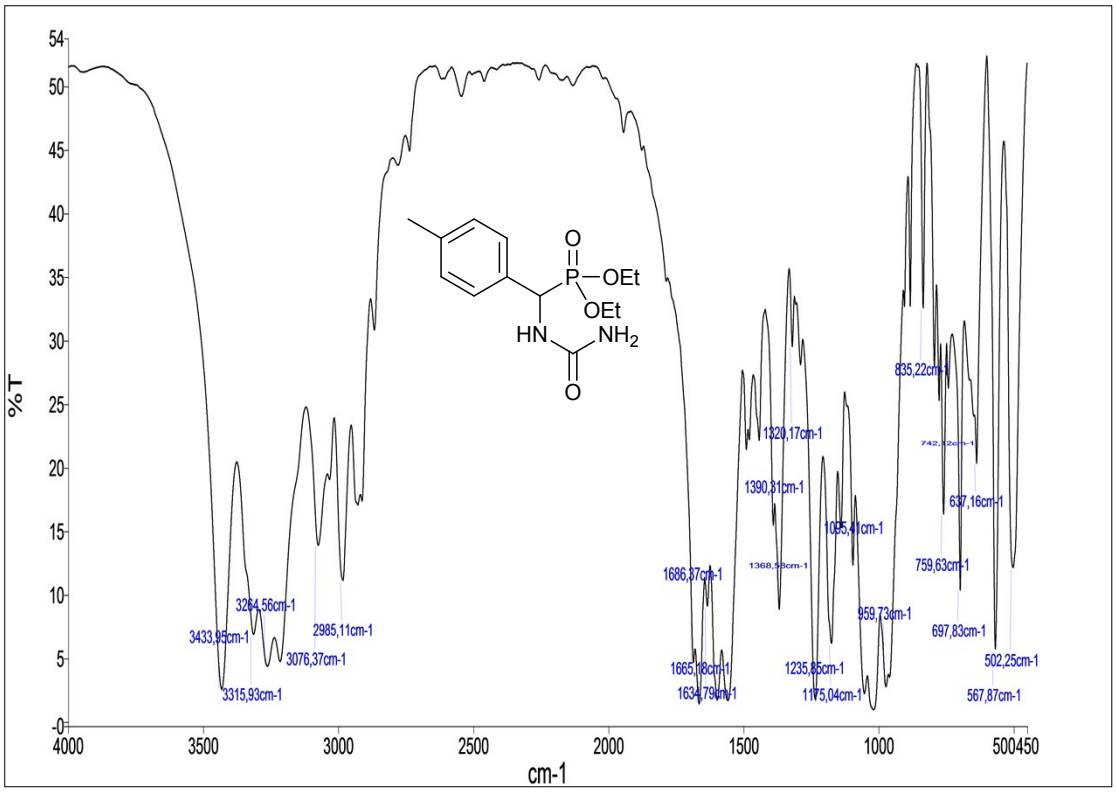
IR spectrum: Diethyl [α-ureido-(phenyl)]methyl phosphonate



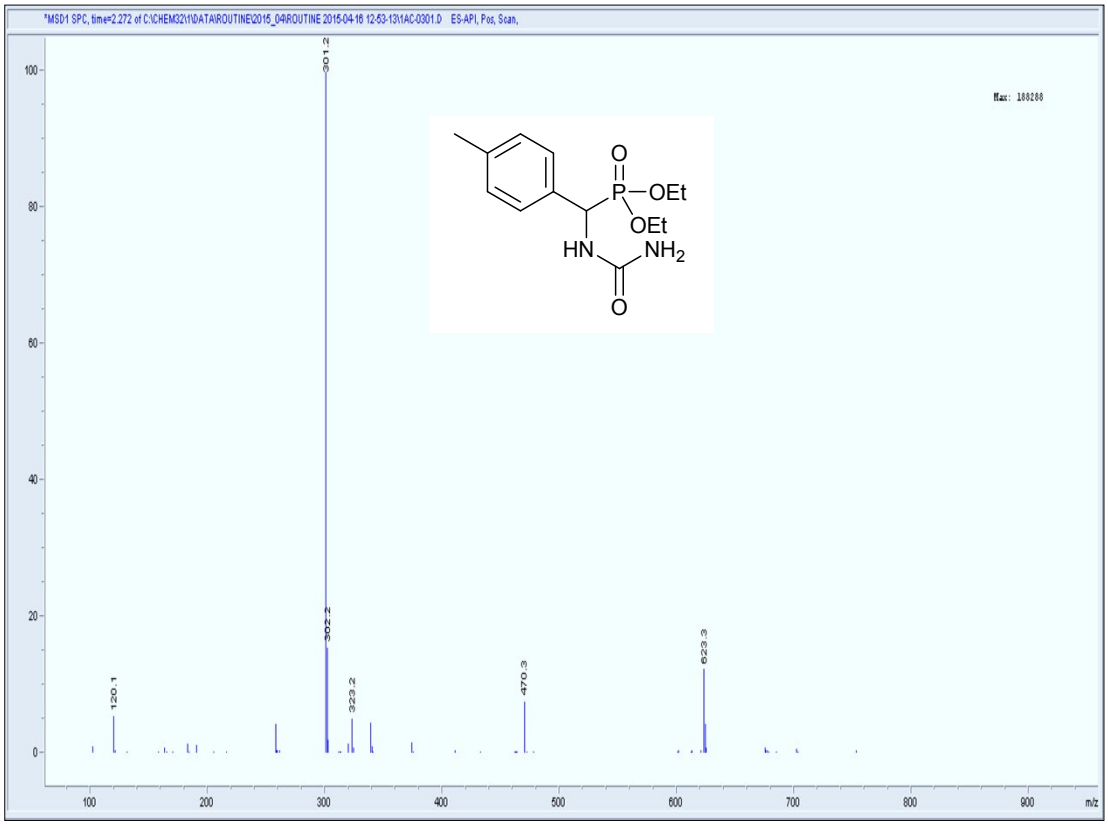
^{1}H NMR spectrum:Diethyl [α-ureido-(4-methylphenyl)]methyl phosphonate



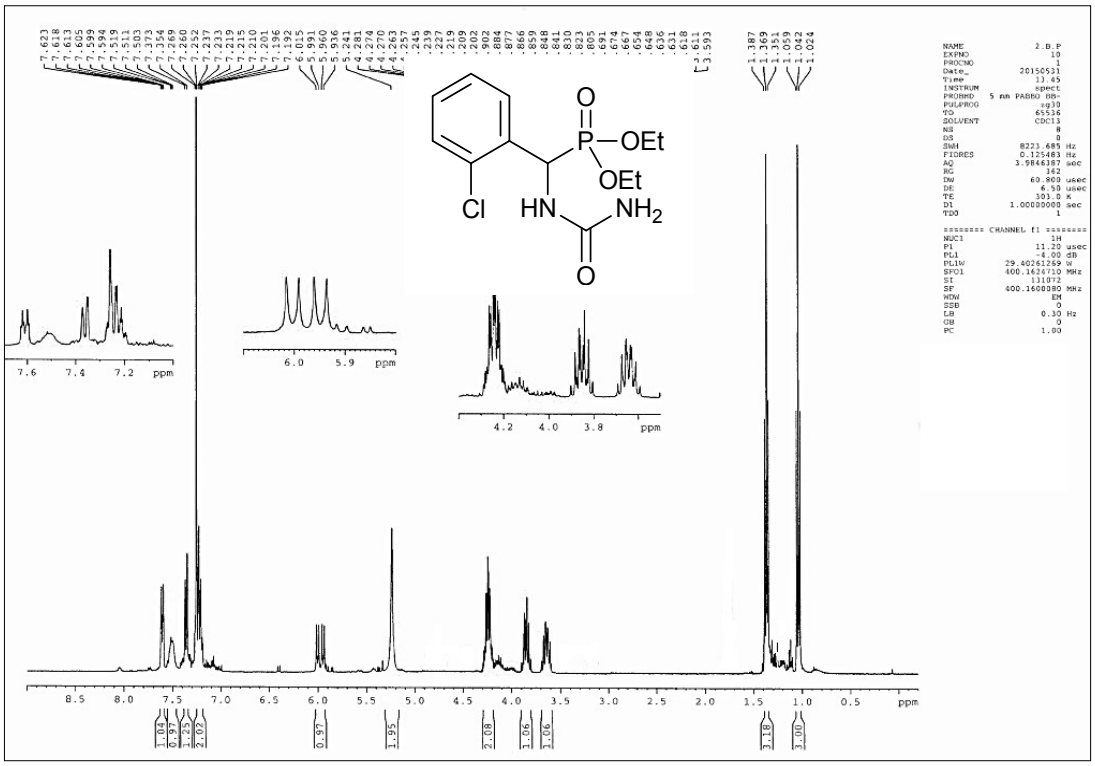
^{31}P NMR spectrum:Diethyl [α-ureido-(4-methylphenyl)]methyl phosphonate



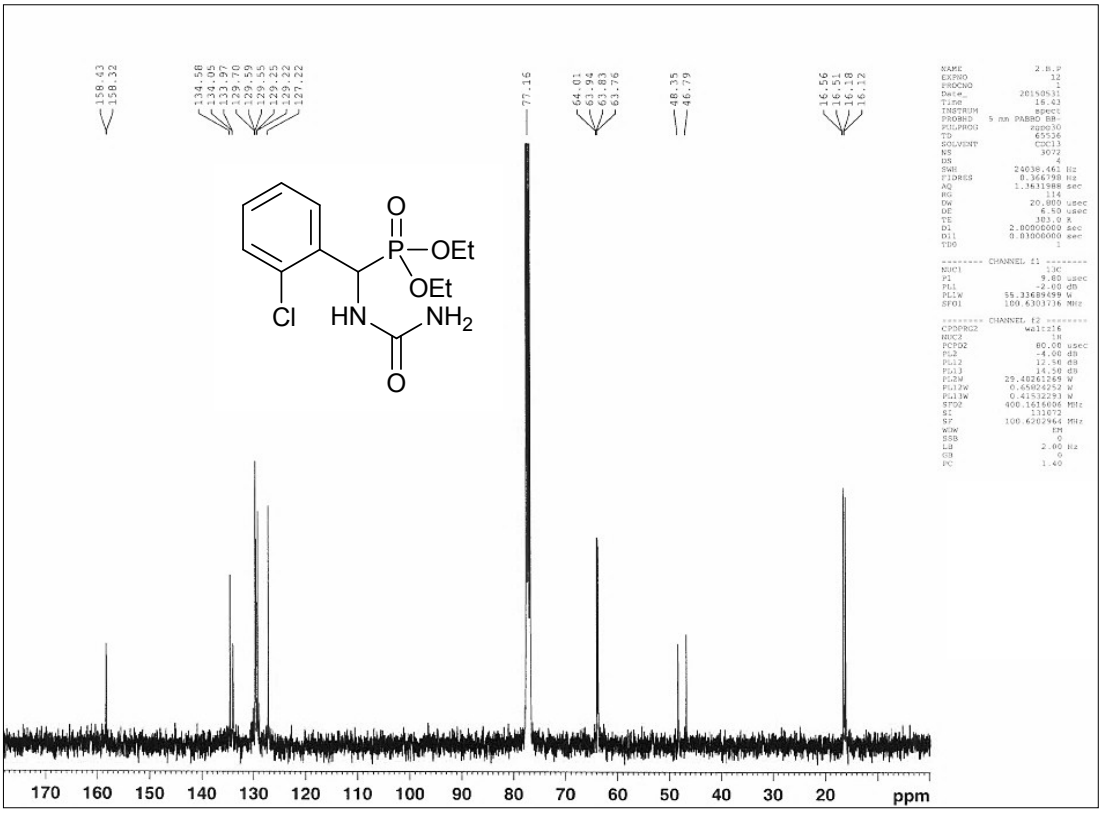
IR spectrum:Diethyl [α-ureido-(4-methylphenyl)]methyl phosphonate



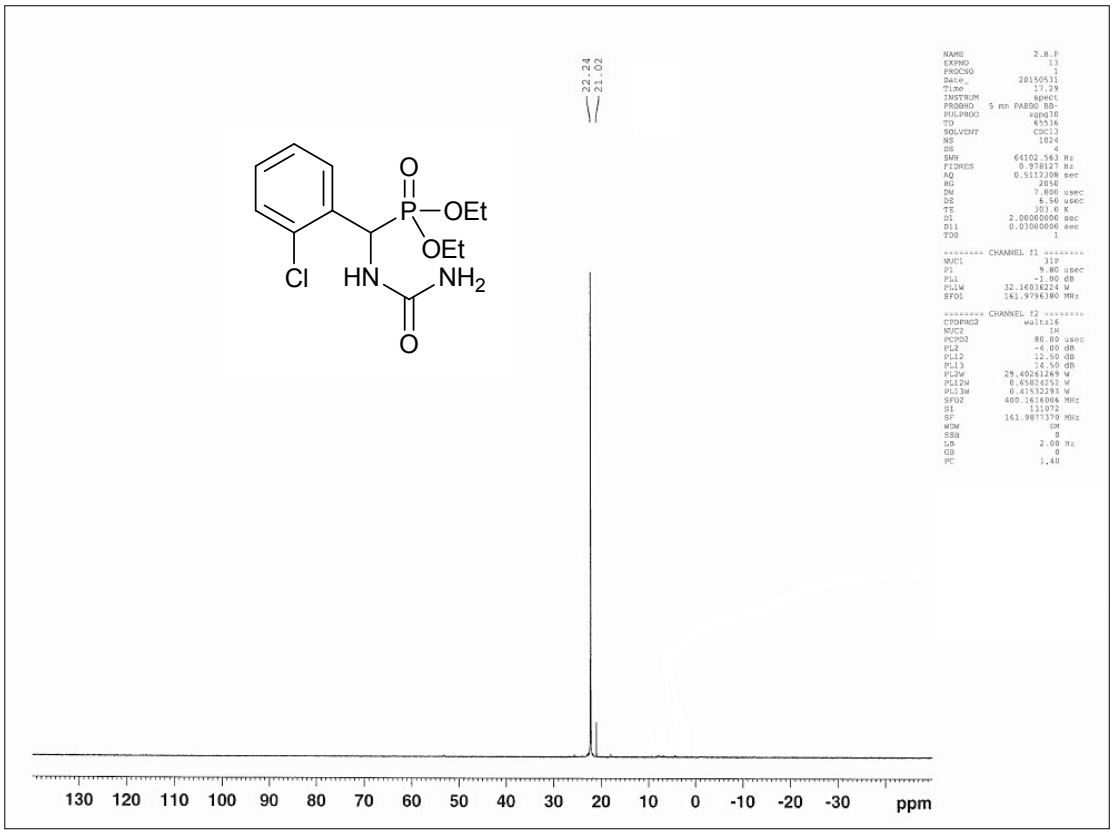
MS:Diethyl [α-ureido-(4-methylphenyl)]methyl phosphonate



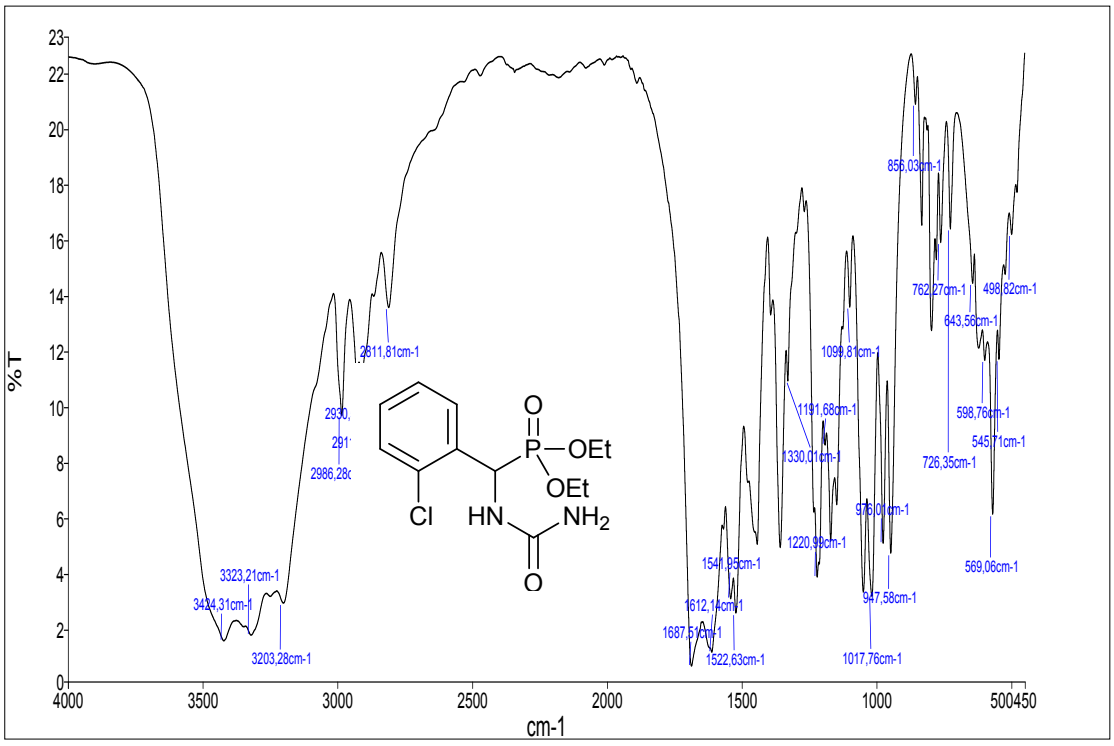
^{1}H NMR spectrum:Diethyl [α-ureido-(2-chlorophenyl)]methyl phosphonate



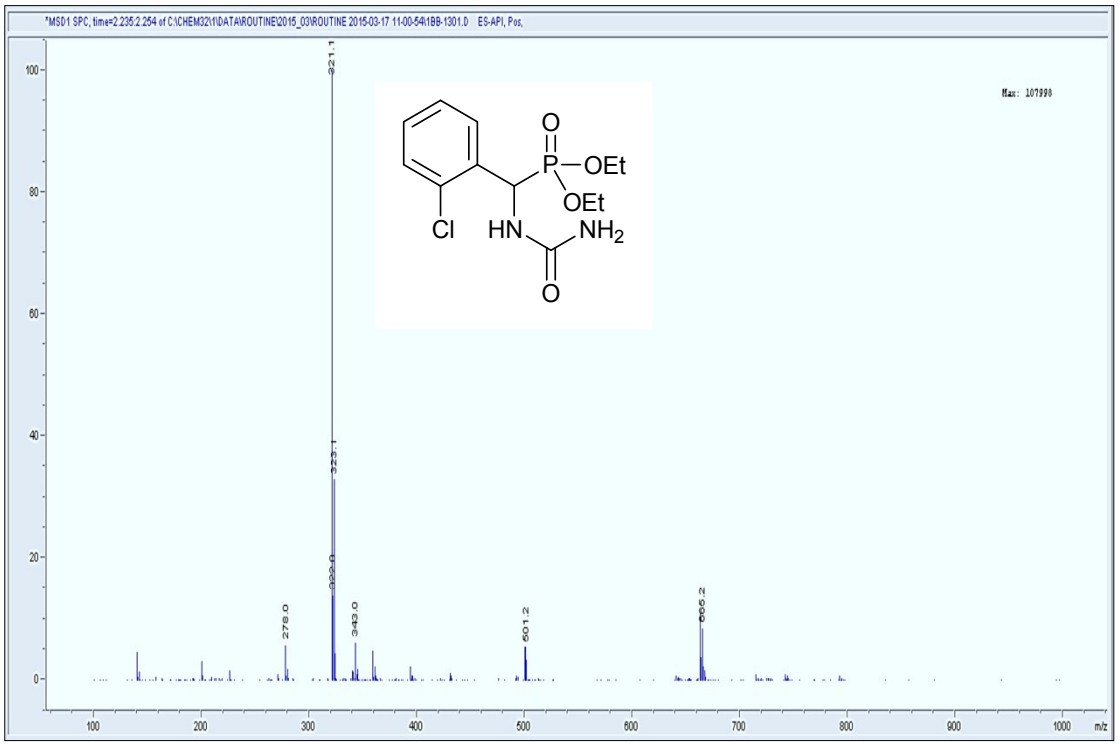
^{13}C NMR spectrum:Diethyl [α-ureido-(2-chlorophenyl)]methyl phosphonate



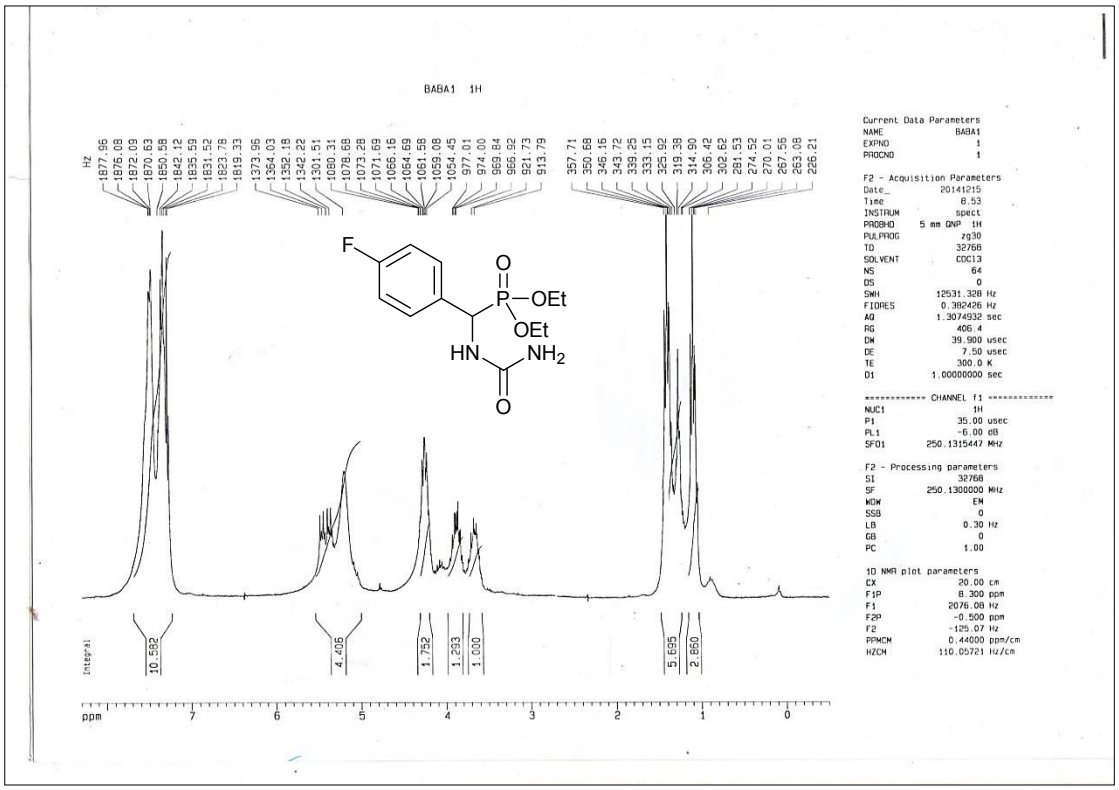
^{31}P NMR spectrum:Diethyl [*α*-ureido-(2-chlorophenyl)]methyl phosphonate



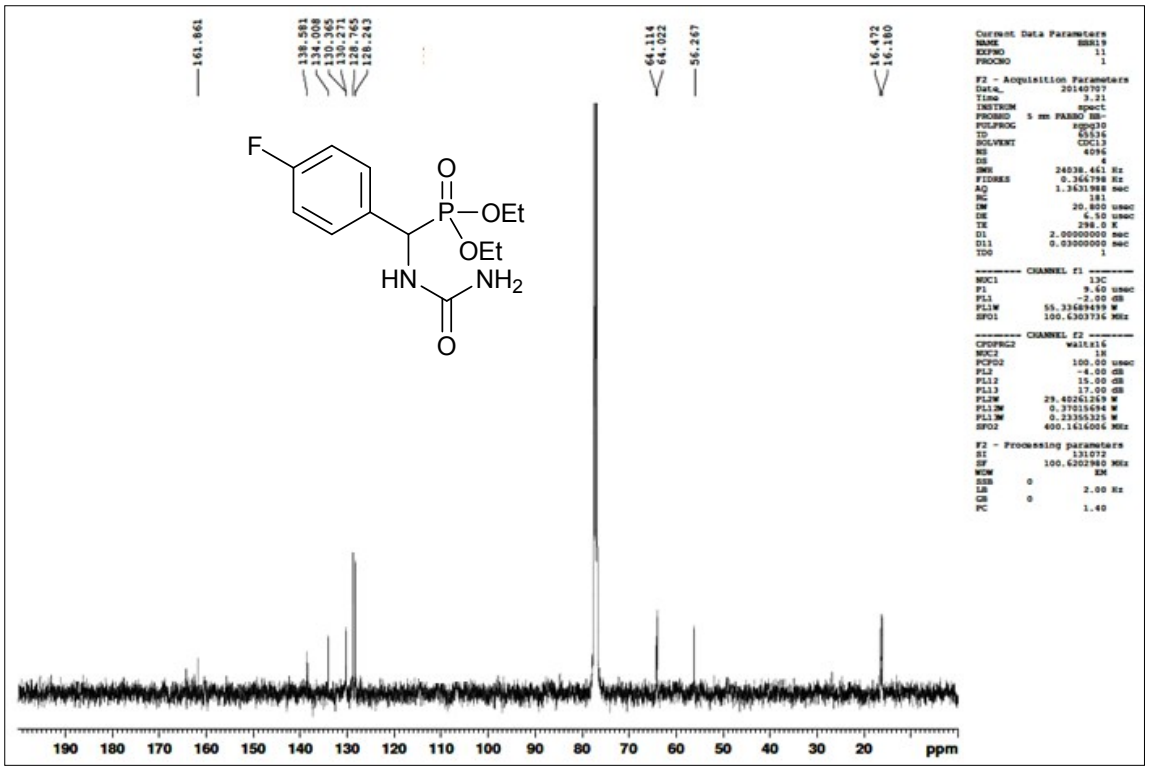
IR spectrum:Diethyl [α-ureido-(2-chlorophenyl)]methyl phosphonate



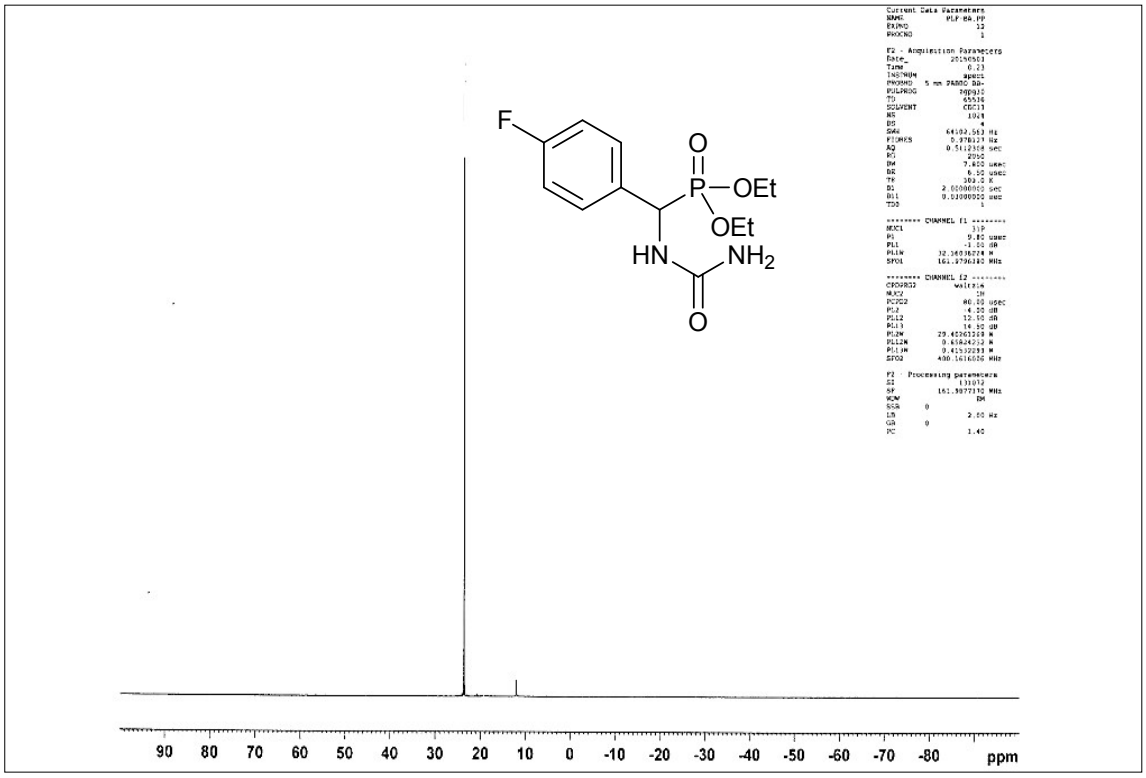
MS:Diethyl [*α*-ureido-(2-chlorophenyl)]methyl phosphonate



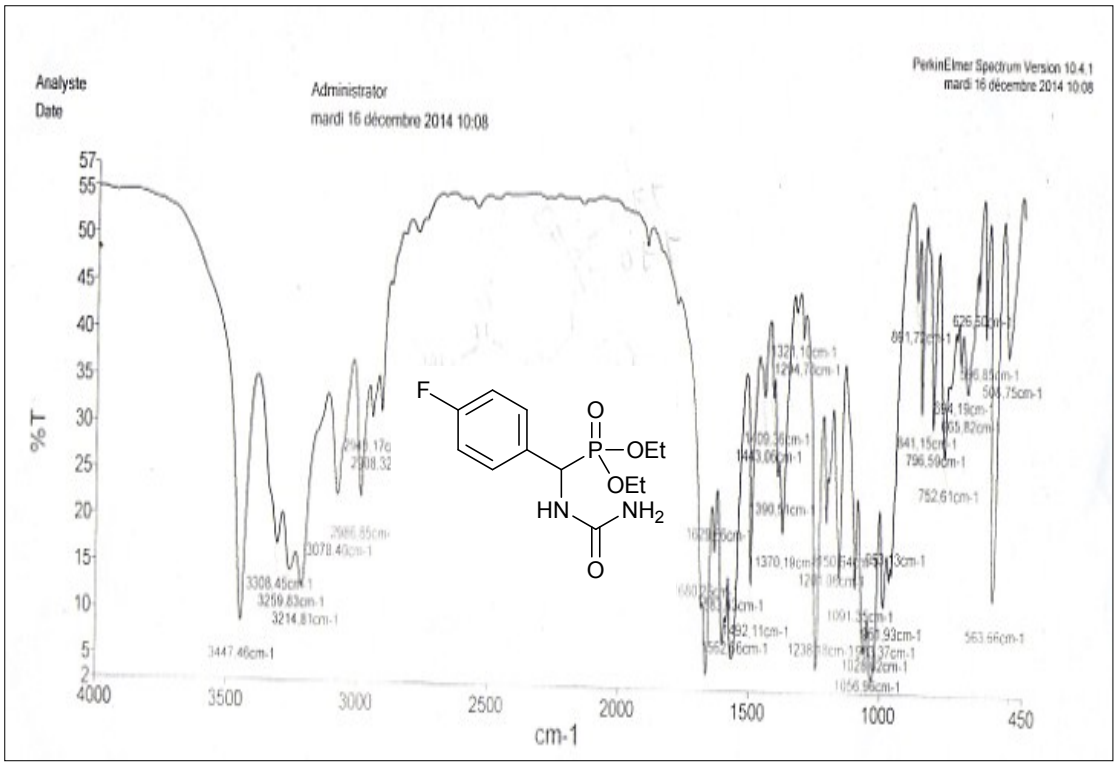
^{1}H NMR spectrum: Diethyl [α-ureido-(4-fluorophenyl)] methyl phosphonate



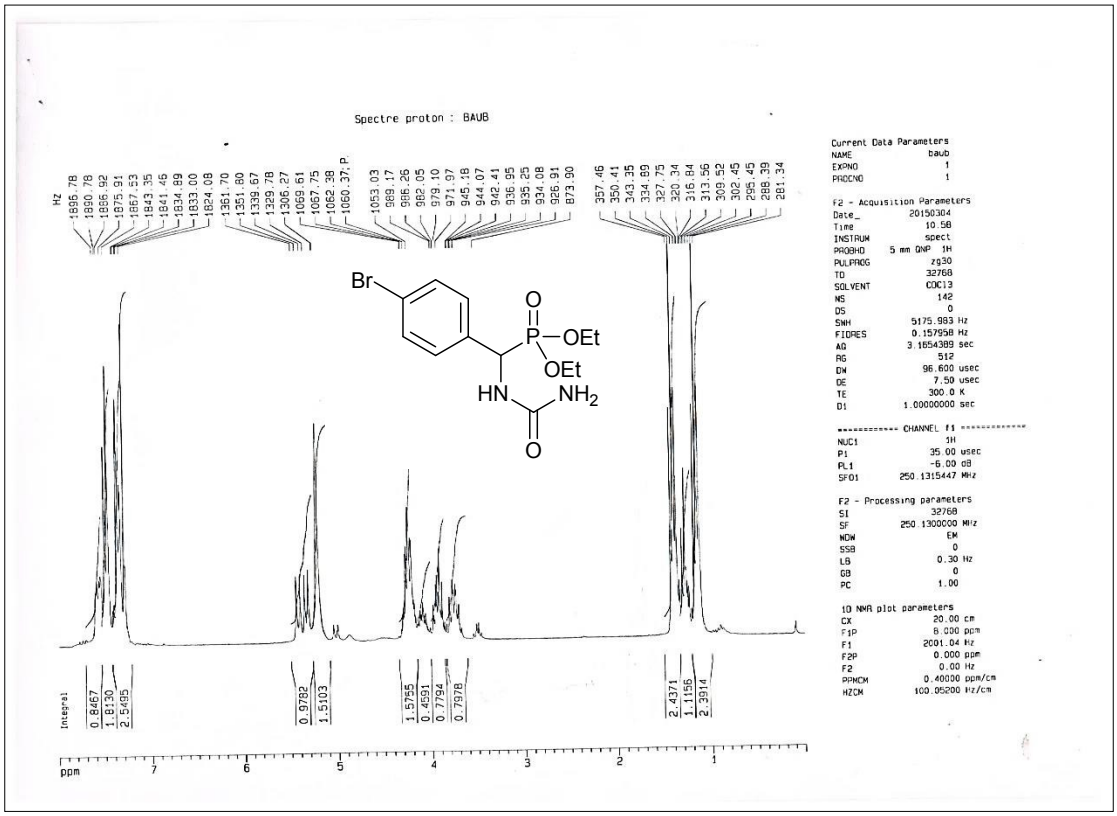
^{13}C NMR spectrum: Diethyl [α-ureido-(4-fluorophenyl)] methyl phosphonate



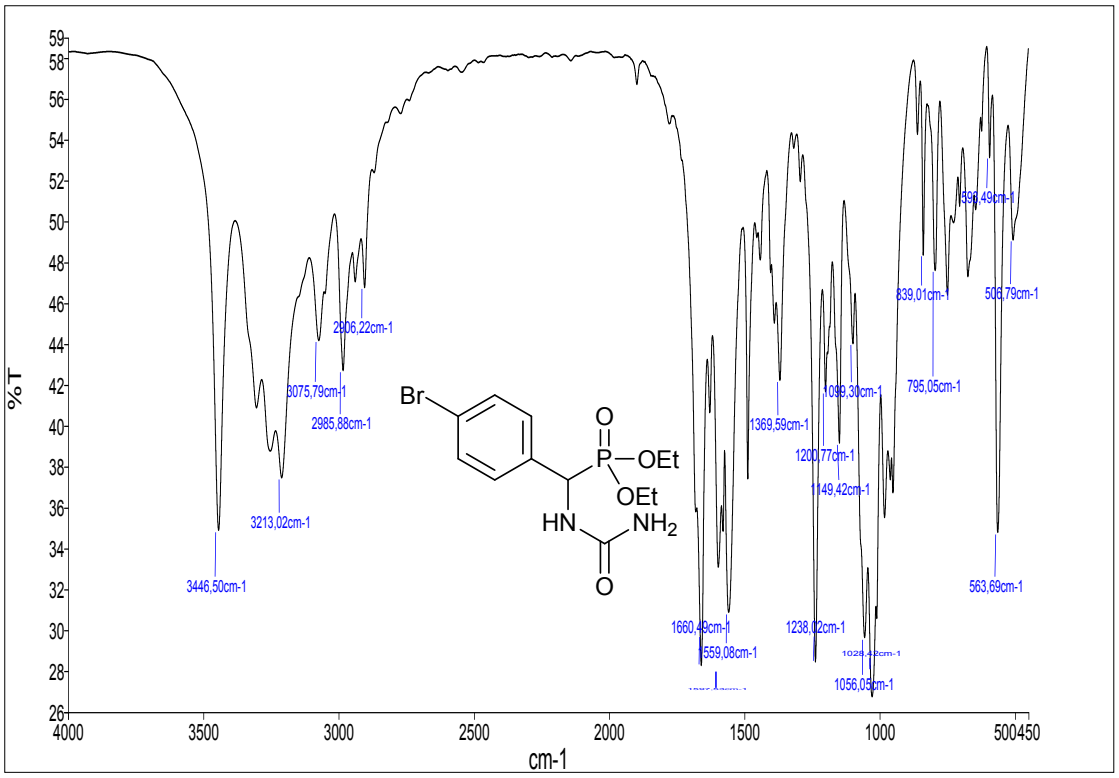
^{31}P NMR spectrum: Diethyl [α-ureido-(4-fluorophenyl)] methyl phosphonate



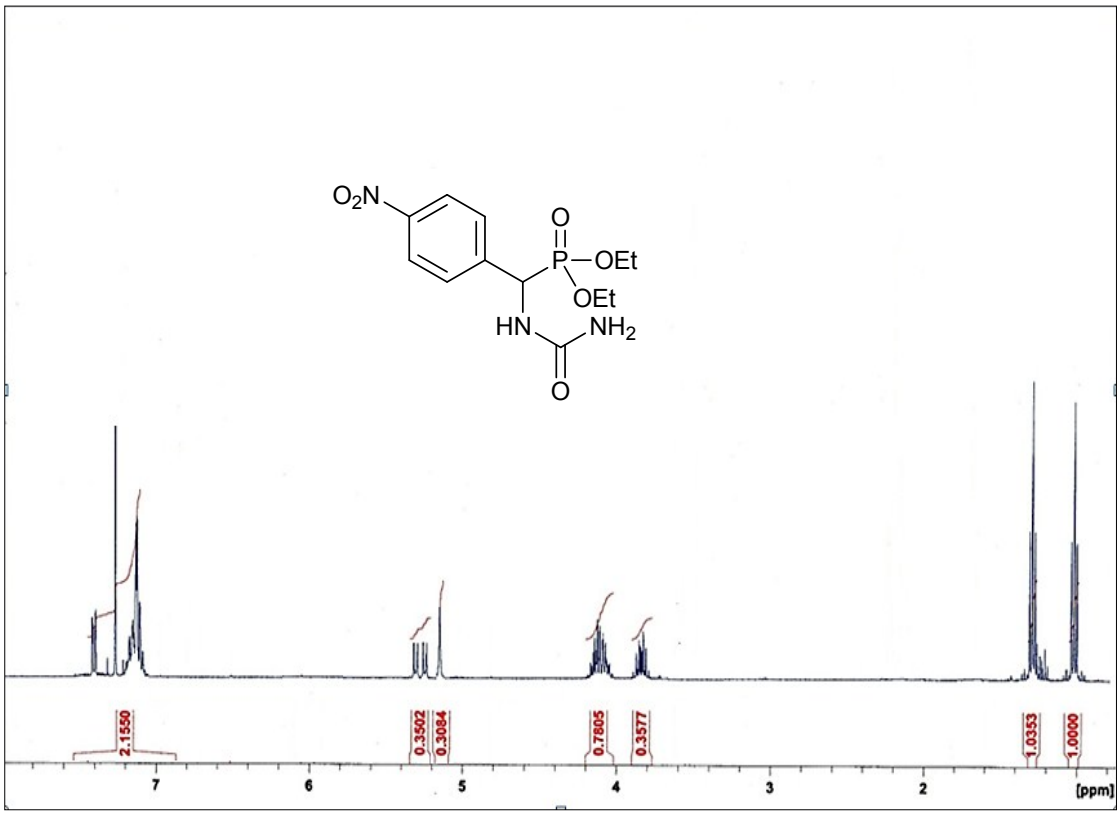
IR spectrum: Diethyl [α-ureido-(4-fluorophenyl)] methyl phosphonate



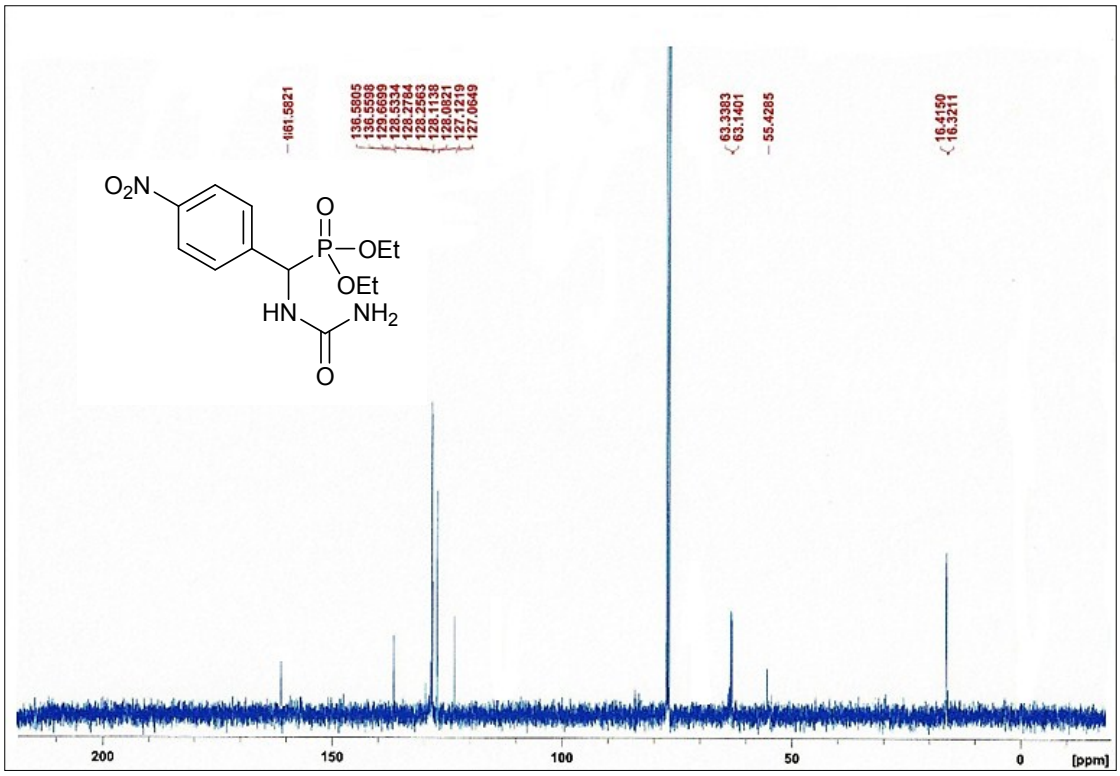
^{1}H NMR spectrum: Diethyl [α-ureido-(4-bromophenyl)] methyl phosphonate



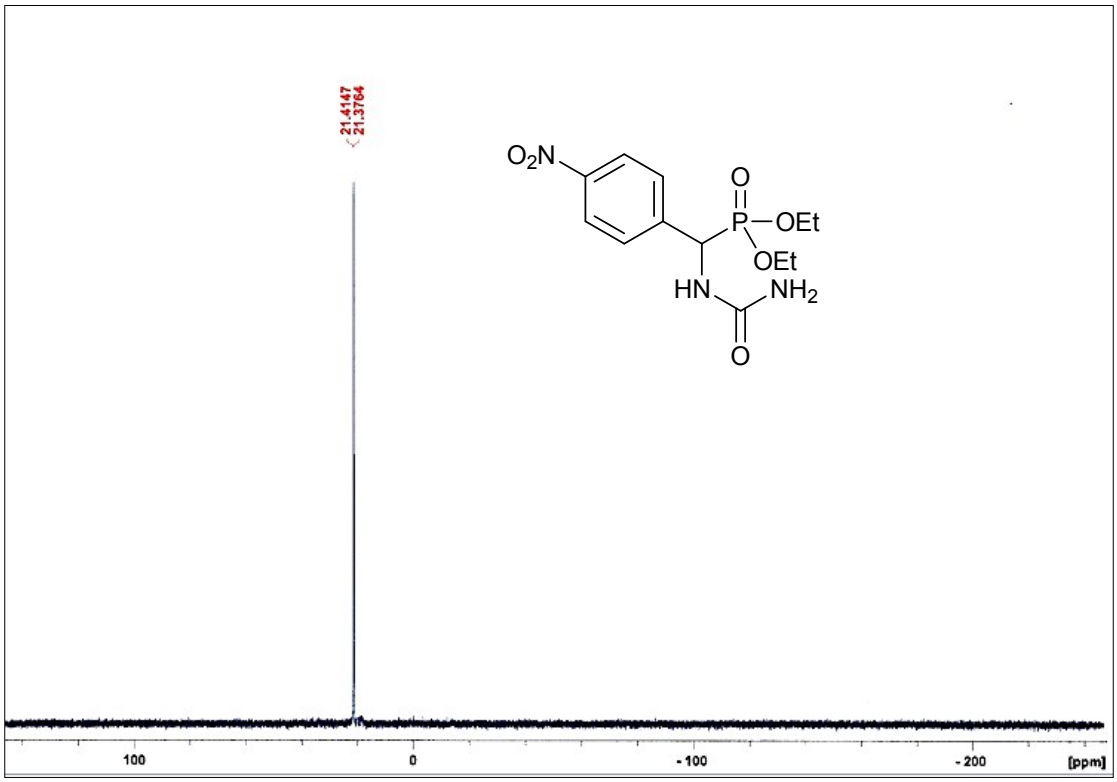
IR spectrum:Diethyl [α-ureido-(4-bromophenyl)] methyl phosphonate



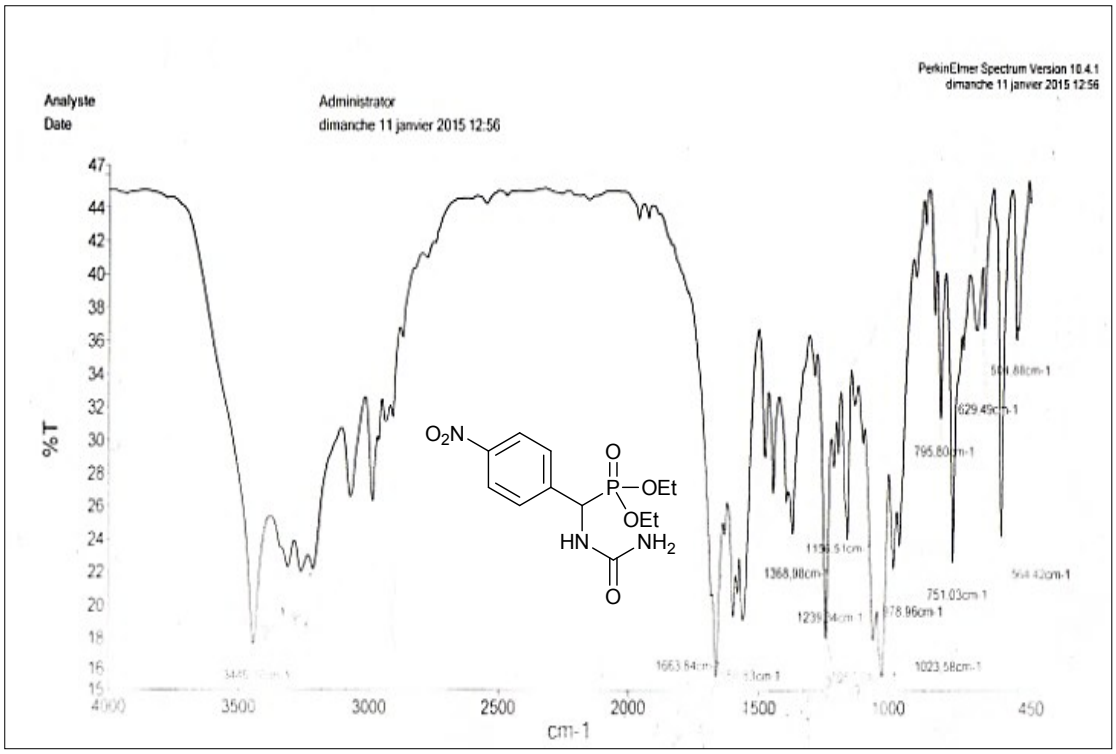
^{1}H NMR spectrum:Diethyl [α-ureido-(4-nitrophenyl)] methyl phosphonate



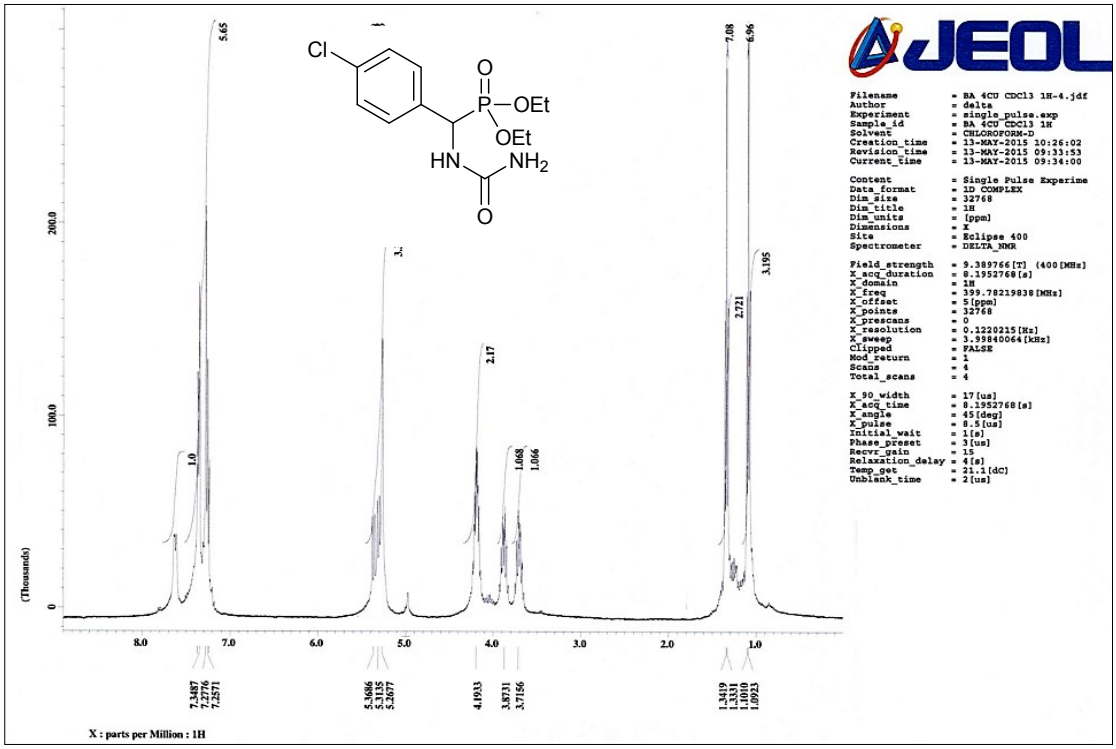
^{13}C NMR spectrum:Diethyl [α-ureido-(4-nitrophenyl)] methyl phosphonate



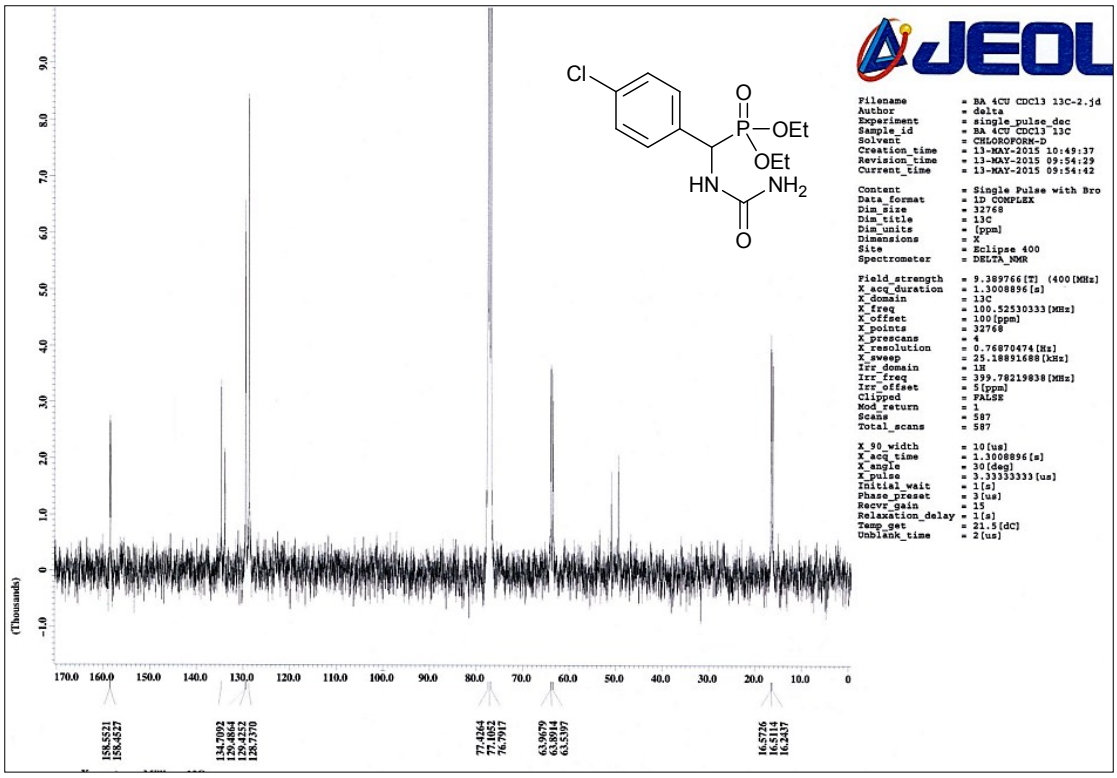
^{31}P NMR spectrum:Diethyl [α-ureido-(4-nitrophenyl)] methyl phosphonate



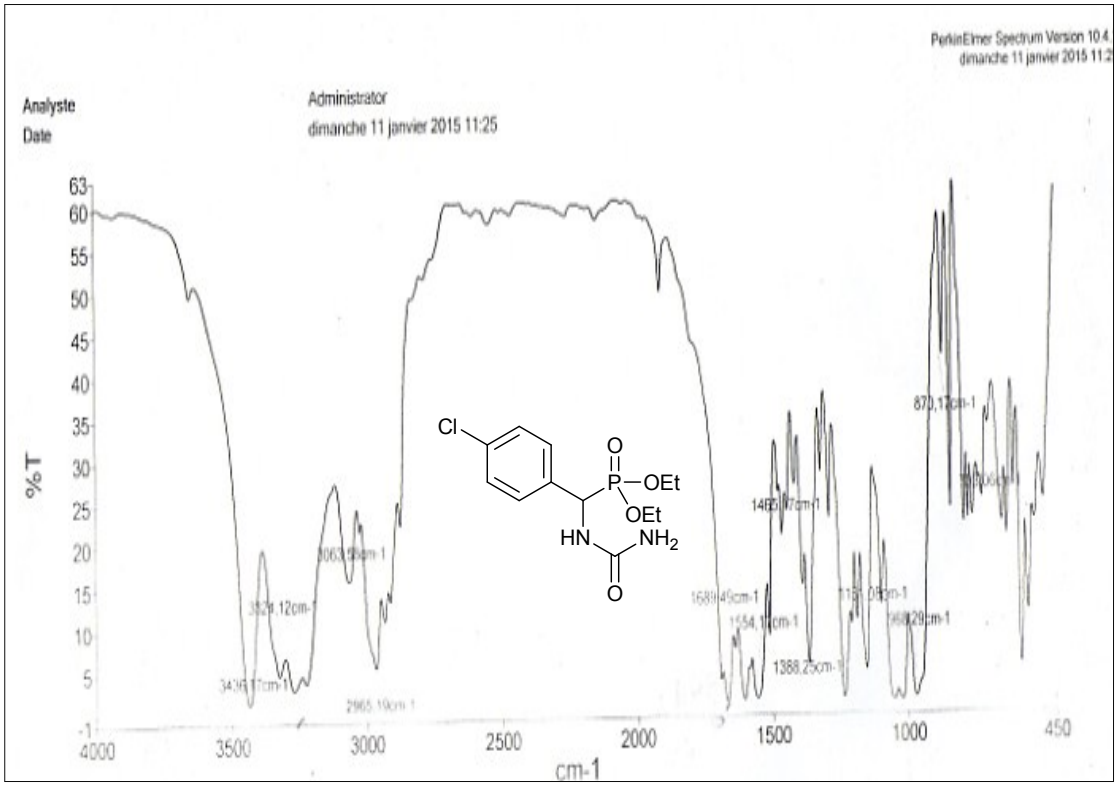
IR spectrum:Diethyl [α-ureido-(4-nitrophenyl)] methyl phosphonate



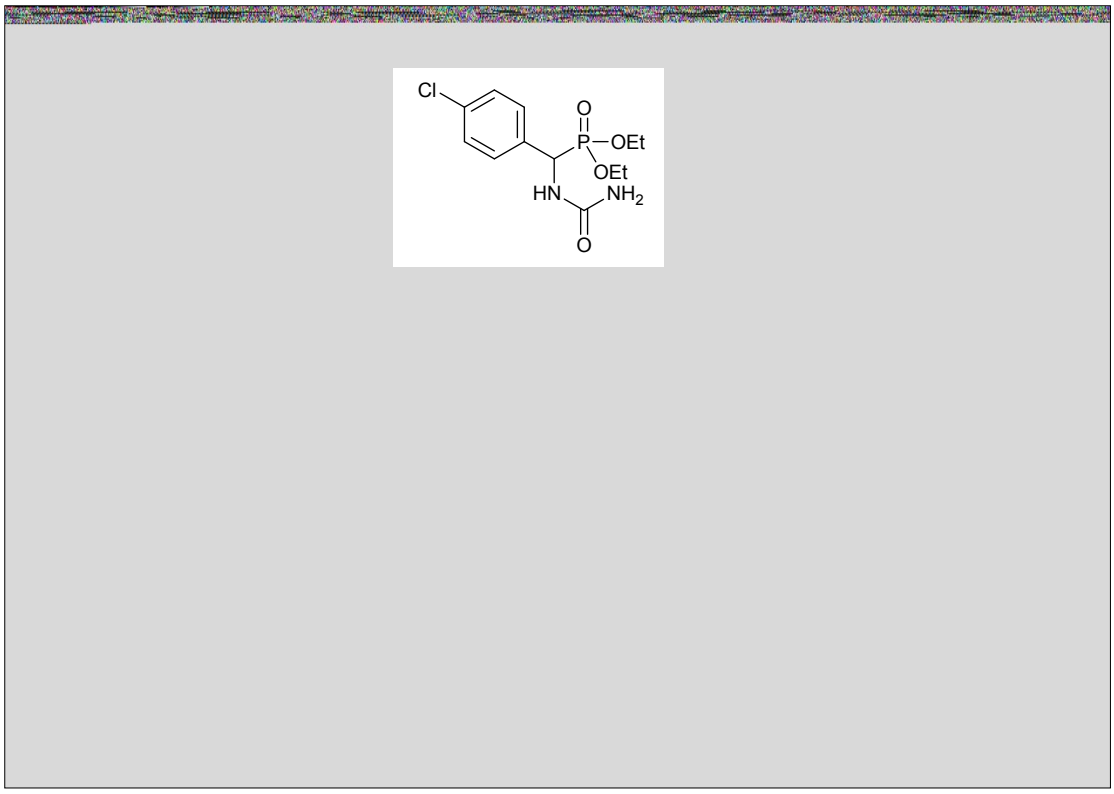
^{1}H NMR spectrum:Diethyl [α-ureido-(4-chlorophenyl)] methyl phosphonate



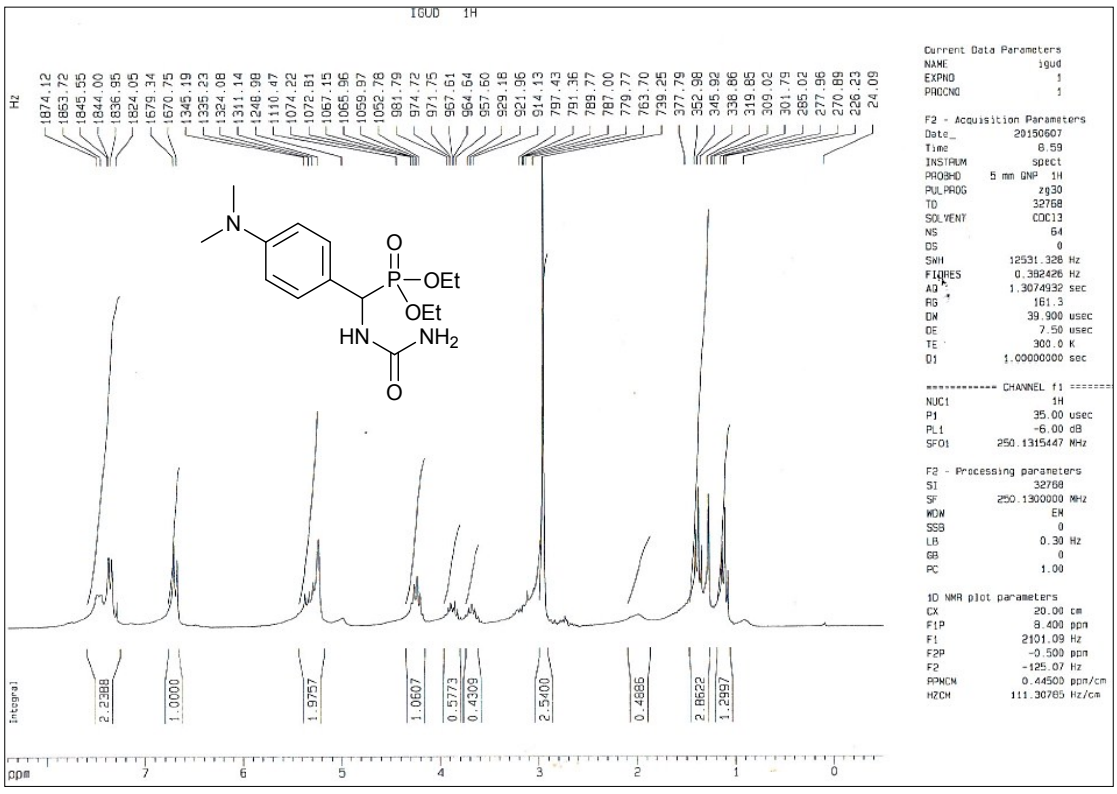
^{13}C NMR spectrum:Diethyl [α-ureido-(4-chlorophenyl)] methyl phosphonate



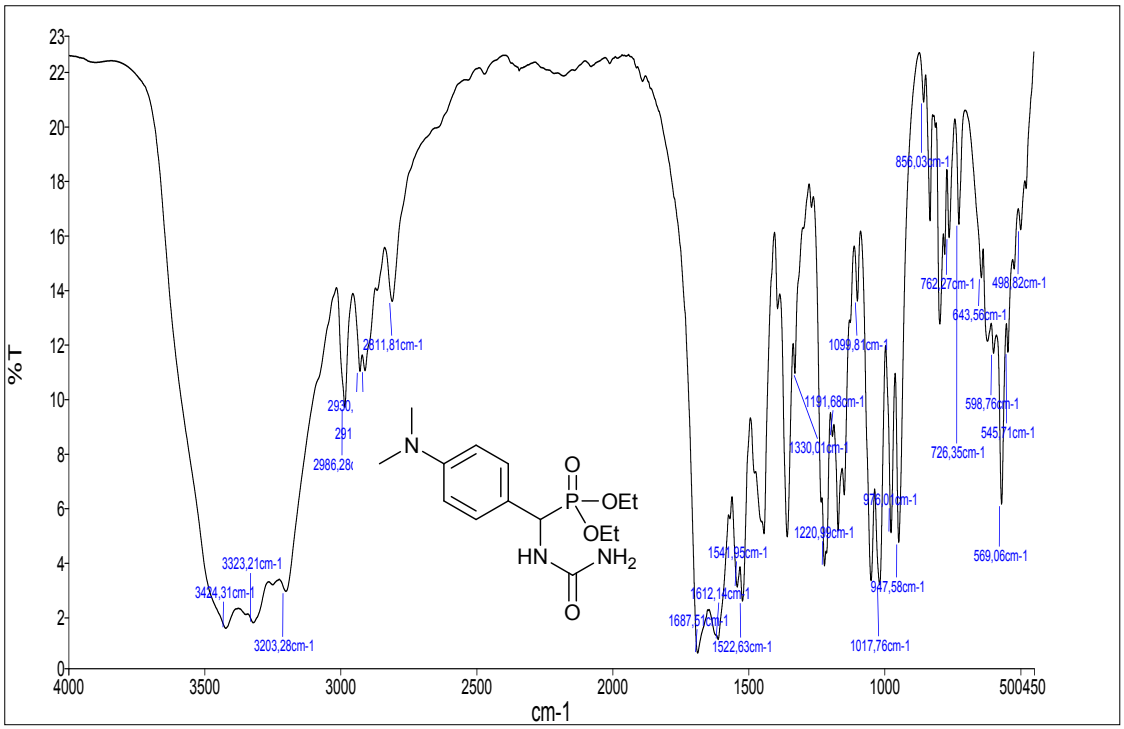
IR spectrum:Diethyl [α-ureido-(4-chlorophenyl)] methyl phosphonate



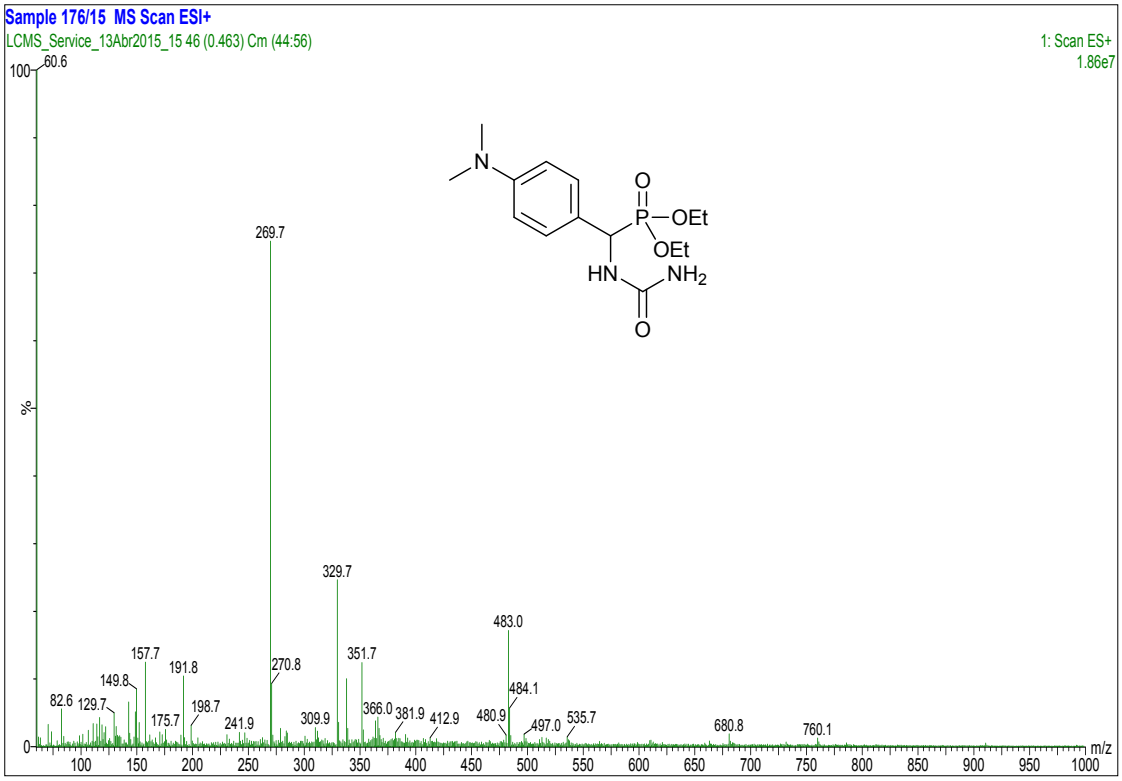
MS:Diethyl [α-ureido-(4-chlorophenyl)] methyl phosphonate



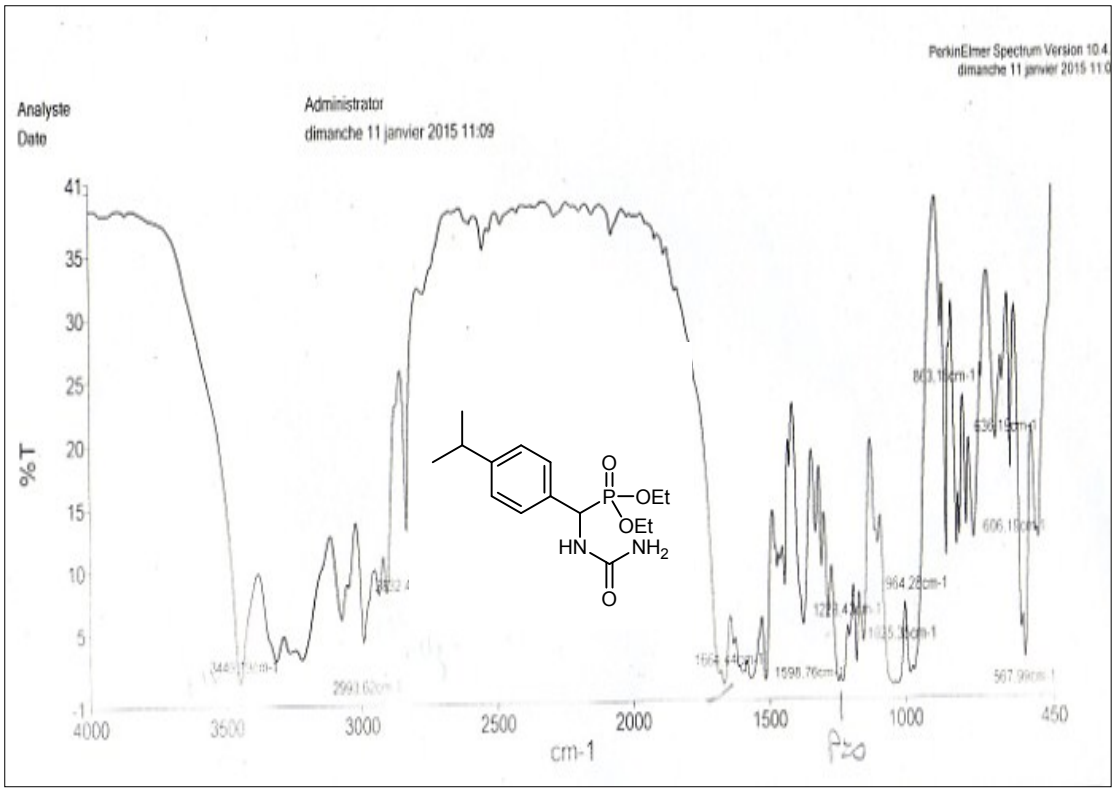
^{1}H RMN:Diethyl [α-ureido-(4-dimethylamino)phenyl)] methyl phosphonate



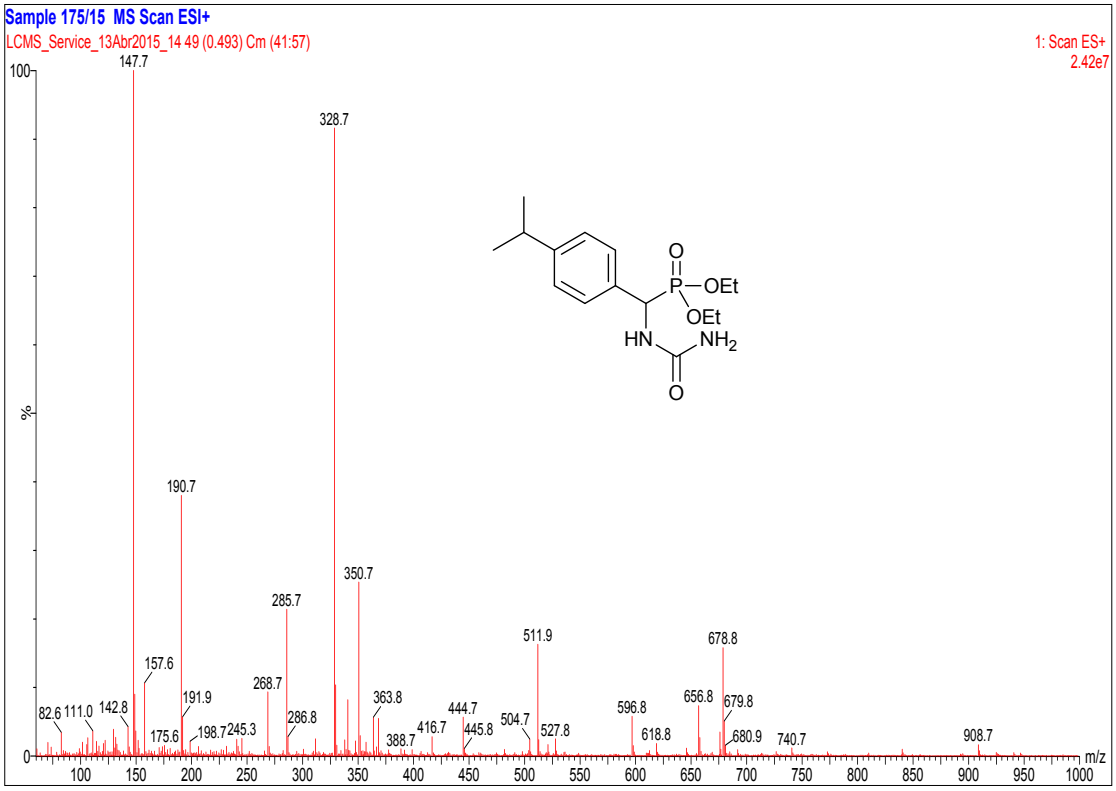
IR spectrum:Diethyl [α-ureido-(4-dimethylamino)phenyl)] methyl phosphonate



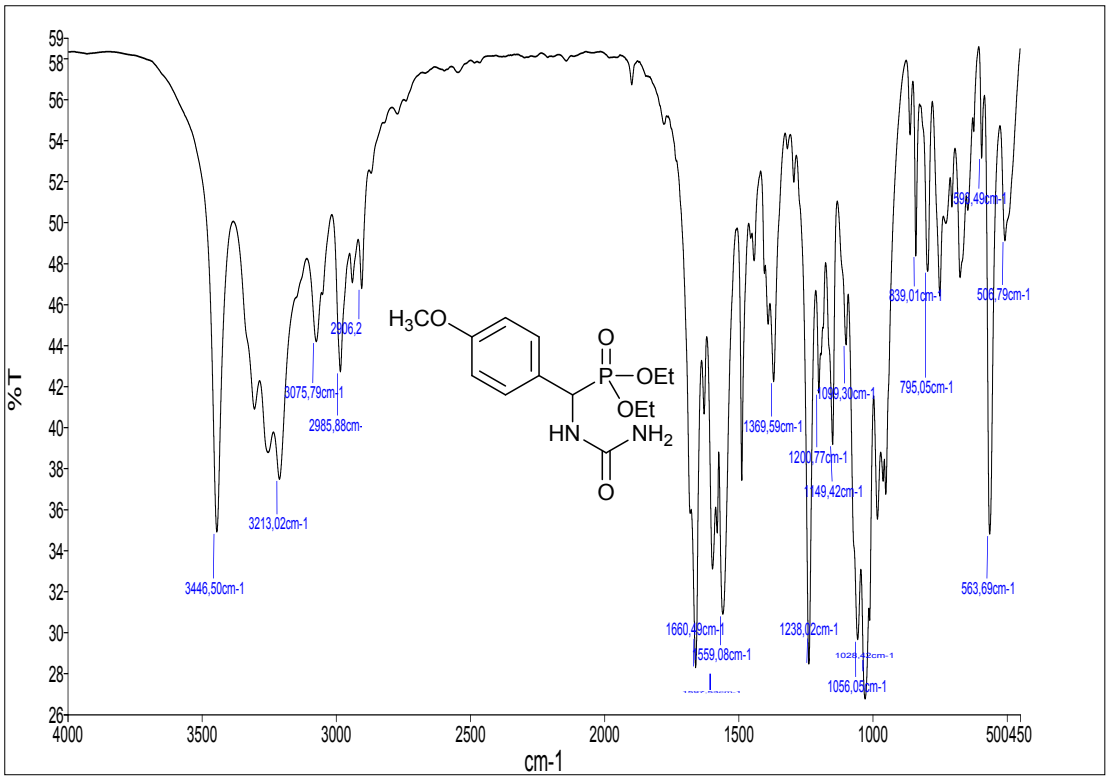
MS:Diethyl [α-ureido-(4-dimethylamino)phenyl)]methyl phosphonate



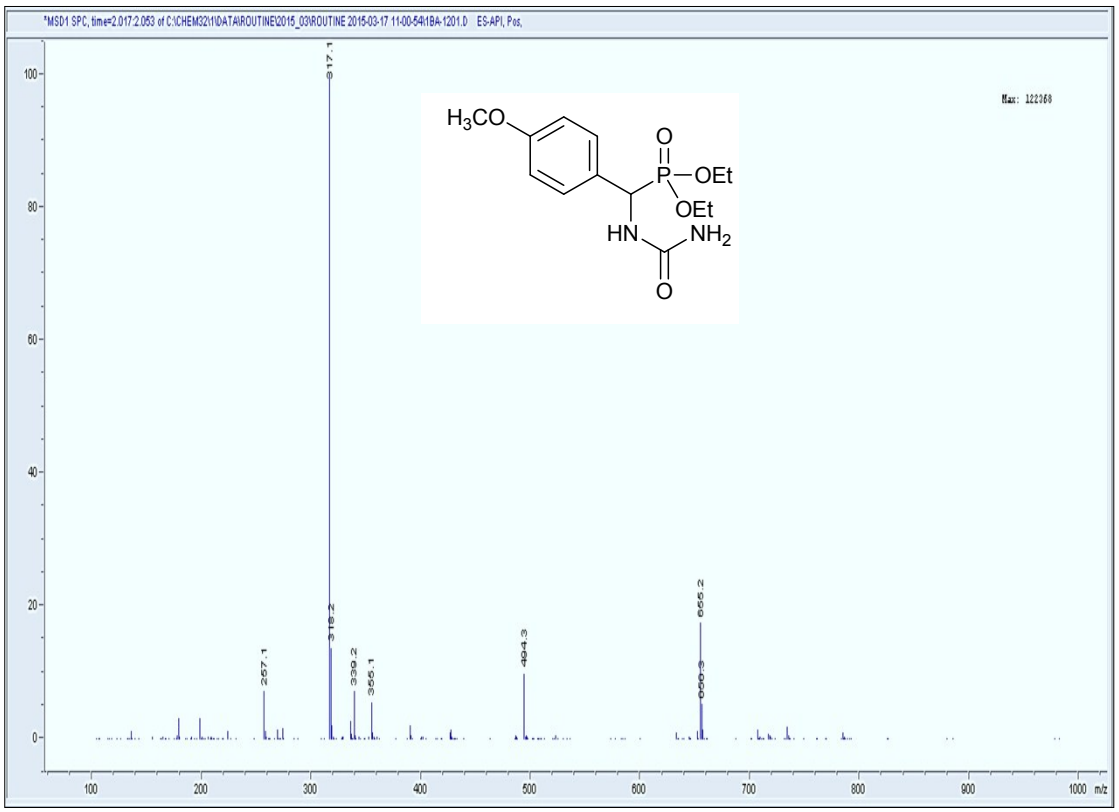
IR spectrum:Diethyl [α-ureido-(4-isopropylphenyl)]methyl phosphonate



MS:Diethyl [α-ureido-(4-isopropylphenyl)]methyl phosphonate



IR spectrum:Diethyl [α-ureido-(4-methoxyphenyl)]methyl phosphonate



MS:Diethyl [α-ureido-(4-methoxyphenyl)]methyl phosphonate