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A catalyst-free one-step synthesis of *N*-pyrimidinyl amidines from endocyclic enamines and 4-azidopyrimidines

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Table of contents

General information

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance II spectrometr at 400 and 100 MHz, respectively, with $SiMe_4$ as internal reference in $CDCl_3$; the chemical shifts (δ) were expressed in ppm, and *J* values were given in Hz. Mass spectra were recorded with Shimadzu GCMS-QP2010 Ultra instrument in electron ionization (EI) mode with direct sample introduction into the ion source. Electron energy - 70eV. The compounds were analyzed in positive ion detection mode. The IR spectra were recorded with a FT-IR ATR (attenuated total reflection, ZnSe) Bruker Alpha IR-Fur spectrometer in the 4000−400 cm^{-1} region. Microanalyses were performed out using a CHNS/O analyser. The reactions were monitored by analytical TLC on aluminium foil plates with 0.2 mm silica gel with a fluorescent indicator visualized under UV light. The column chromatography was performed with 60−120 mesh silica gel. All melting points were determined with a Stuart SMP3 apparatus and are uncorrected.

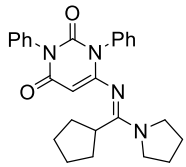
Azides **1a,b** were prepared following the literature: (*a*) P. J. Bhuyan, H. N. Borah and J. S. Sandhu, *J. Chem. Soc., Perkin Trans. 1*, 1999, 3083; (*b*) M. Sako, S. Ohara, K. Hirota, K. Kano, Y. Maki and E. C. Taylor, *J. Org. Chem.*, 1991, **56**, 6302.

Enamines **2**, apart from **2f**, were commercially available.

XRD analyses were performed on Xcalibur 3 diffractometer on standard procedure (MoK_α radiation, graphite monochromator, T = 295(2) K, ω-scans with the step 1°). Empirical absorption correction was applied. The structures were solved with the Superflip [L. Palatinus and G. Chapuis, *J. Appl. Crystallogr*., 2007, **40**, 786] structure solution program using Charge Flipping and refined with the ShelXL [G. M. Sheldrick, *Acta Crystallogr*., 2008, **A64**, 112] refinement package using Least Squares minimisation in the Olex2 program package [O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr*., 2009, **42**, 339].

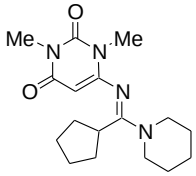
Analytical data for amidines 3b-e

*6-{[(E)-Cyclopentyl(pyrrolidin-1-yl)methylidene]amino}-1,3-diphenylpyrimidine-2,4(1H,3H)-dione (**3b**).*



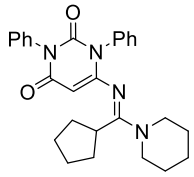
Yield 180 mg (42%), colourless powder, mp 191–193 °C, R_f 0.63 (chloroform–ethanol, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.48–1.70 (m, 6H, $3CH_2^{cyclopent}$), 1.73–1.84 (m, 2H, $CH_2^{cyclopent}$), 1.90 (t, *J* 6.3 Hz, 4H, $2CH_2^{pyrrol}$), 2.91 (p, *J* 7.9 Hz, 1H, $CH^{cyclopent}$), 3.36 (br. s, 4H, $2NCH_2^{pyrrol}$), 4.86 (s, 1H, CH^{pyrim}), 7.21–7.27 (m, 2H, $2CH^{Ph}$), 7.29–7.43 (m, 6H, $6CH^{Ph}$), 7.43–7.51 (m, 2H, $2CH^{phenyl}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.2 (CH_2^{pyrrol}), 26.1 ($2CH_2^{cyclopent}$), 30.6 ($2CH_2^{cyclopent}$), 42.9 ($CH^{cyclopent}$), 49.2 ($2NCH_2^{pyrrol}$), 84.4 (CH^{pyrim}), 127.9 (CH^{Ph}), 128.0 (CH^{Ph}), 128.6 (CH^{Ph}), 128.8 (CH^{Ph}), 128.9 (CH^{Ph}), 129.2 (CH^{Ph}), 135.9 (C^{Ph}), 137.3 (C^{Ph}), 152.3 (C=O), 155.8 ($C4^{pyrim}$), 163.4 (C=O), 163.5 ($C^{amidine}$). MS (EI), m/z (%): 428 ($[M]^+$, 100), 217 (48), 119 (100), 91 (74). IR (NPVO, ZnSe, cm^{-1}): ν 1328, 1361, 1384, 1450, 1493, 1536, 1578, 1647, 1701, 2949, 2875. Anal. Calcd (%) for $C_{26}H_{28}N_4O_2$: C, 72.87; H, 6.59; N, 13.07. Found: C, 72.48; H, 6.85; N, 13.20.

*6-{[(E)-Cyclopentyl(piperidin-1-yl)methylidene]amino}-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (**3c**).*



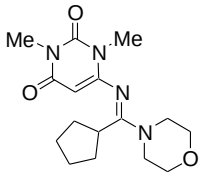
Yield 200 mg (63%), colourless powder, mp 113–115 °C, R_f 0.42 (ethyl acetate–ethanol, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.55–1.85 (m, 12H, $3CH_2^{cyclopent}$ + $3CH_2^{piper}$), 1.85–1.99 (m, 2H, $CH_2^{cyclopent}$), 3.05–3.20 (m, 1H, $CH_2^{cyclopent}$), 3.27 (s, 3H, NCH_3), 3.33 (s, 3H, NCH_3), 3.41–3.55 (m, 4H, $2NCH_2^{piper}$), 4.75 (s, 1H, CH^{pyrim}). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.3 (CH_2^{piper}), 26.0 ($2CH_2^{cyclopent}$), 26.2 ($2CH_2^{piper.}$), 27.7 (NCH_3), 30.3 (NCH_3), 31.0 ($2CH_2^{cyclopent.}$), 41.3 ($CH^{cyclopent.}$), 47.5 ($2NCH_2^{piper}$), 84.6 ($CH^{pyrim.}$), 152.9 (C=O), 157.0 ($C4^{pyrim.}$), 163.6 (C=O), 163.7 ($C^{amidine}$). MS (EI), m/z (%): 318 ($[M]^+$, 28), 277 (20), 235 (12), 140 (100), 84 (56), 55 (50). IR (NPVO, ZnSe, cm^{-1}): ν 964, 991, 1017, 1159, 1179, 1270, 1349, 1418, 1560, 1591, 1636, 1693, 2859, 2928. Anal. Calcd (%) for $C_{17}H_{26}N_4O_2$: C, 64.12; H, 8.23; N, 17.60. Found: C, 64.16; H, 8.25; N, 17.33.

*6-{[(E)-Cyclopentyl(piperidin-1-yl)methylidene]amino}-1,3-diphenylpyrimidine-2,4(1H,3H)-dione (**3d**).*

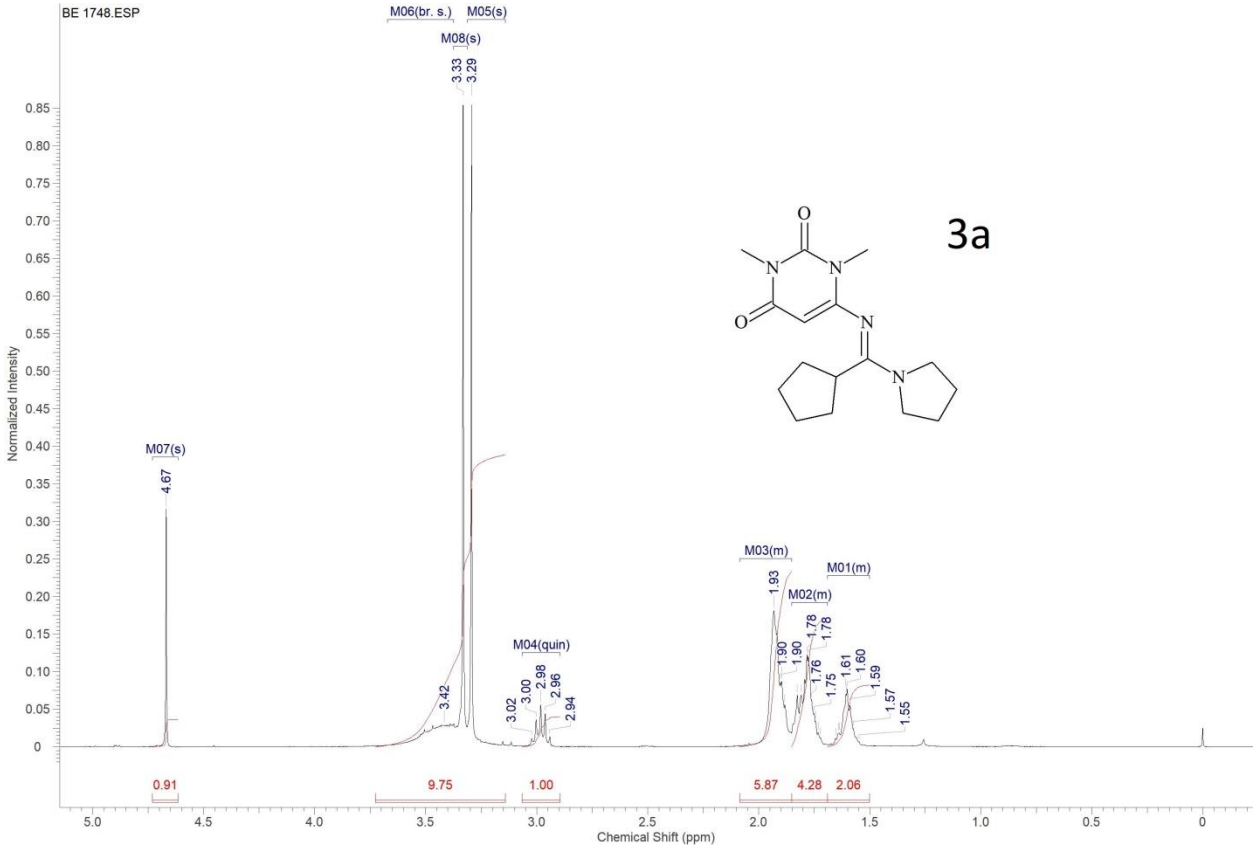


Yield 239 mg (54%), colourless powder, mp 212–215 °C, R_f 0.62 (ethyl acetate–ethanol, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.39 (br. s, 4H, $2CH_2^{piper}$), 1.49–1.74 (m, 6H, CH_2^{piper} + $2CH_2^{cyclopent}$), 1.80 (br. s, 2H, $CH_2^{cyclopent}$), 1.87–2.08 (m, 2H, $CH_2^{cyclopent}$), 3.13–3.39 (m, 5H, $2NCH_2^{piper}$ + $CH^{cyclopent}$), 4.99 (s, 1H, CH^{pyrim}), 7.23 (d, *J* 7.3 Hz, 2H, $2CH^{Ph}$), 7.30–7.43 (m, 6H, $6CH^{Ph}$), 7.43–7.54 (m, 2H, $2CH^{Ph}$). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 23.6 (CH_2^{piper}), 25.4 ($2CH_2^{cyclopent}$), 25.8 ($2CH_2^{piper}$), 30.4 ($2CH_2^{cyclopent}$), 40.7 ($CH^{cyclopent}$), 46.8 ($2NCH_2^{piper}$), 83.4 (CH^{pyrim}), 127.5 (CH^{Ph}), 127.8 (CH^{Ph}), 128.4 (CH^{Ph}), 128.5 (CH^{Ph}), 129.2 (CH^{Ph}), 136.4 (C^{Ph}), 137.3 (C^{Ph}), 151.4 (C=O), 156.9 ($C4^{pyrim}$), 162.2 (C=O), 162.5 ($C^{amidine}$). MS (EI), m/z (%): 442 ($[M]^+$, 5), 274 (10), 23 (100), 204 (40), 144 (20), 117 (52), 77 (25). IR (NPVO, ZnSe, cm^{-1}): ν 1356, 1544, 1571, 1647, 1691, 2941, 2866. Anal. Calcd (%) for $C_{27}H_{30}N_4O_2$; C, 73.28; H, 6.83; N, 12.66. Found: C, 73.30; H, 7.08; N, 12.51.

*6-{(E)-[Cyclopentyl(morpholin-4-yl)methylidene]amino}-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (**3e**).*



Yield 180 mg (56%), beige powder, mp 125–127 °C, R_f 0.30 (ethyl acetate–ethanol, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.56–1.85 (m, 6H, $3CH_2^{cyclopent}$), 1.85–2.01 (m, 2H, $CH_2^{cyclopent}$), 3.15 (p, *J* 9.22 Hz, 1H, $CH^{cyclopent}$), 3.24 (s, 3H, NCH_3), 3.34 (s, 3H, NCH_3), 3.49–3.61 (m, 4H, $2NCH_2^{morph}$), 3.68–3.80 (m, 4H, $2OCH_2^{morph}$), 4.83 (s, 1H, CH^{pyrim}). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.2 ($2CH_2^{cyclopent}$), 27.7 (NCH_3), 30.4 (NCH_3), 30.9 ($2CH_2^{cyclopent}$), 40.8 ($CH^{cyclopent}$), 46.5 ($2NCH_2^{morph}$), 66.5 ($2OCH_2^{morph}$), 85.6 (CH^{pyrim}), 152.7 (C=O), 157.0 ($C4^{pyrim}$), 163.4 (C=O), 163.6 ($C^{amidine}$). MS (EI), m/z (%): 320 ($[M]^+$, 4), 140 (17), 82 (100), 55 (65). IR (NPVO, ZnSe, cm^{-1}): ν 1165, 1261, 1281, 1415, 1569, 1592, 1638, 1693, 2960, 2856. Anal. Calcd (%) for $C_{16}H_{24}N_4O_3$: C, 59.98; H, 7.55; N, 17.49. Found: C, 60.35; H, 7.70; N, 17.78.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M02(m)
M04(quin)
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3.02
3.00
2.98
2.96
2.94
1.93
1.90
1.90
1.78
1.78
1.76
1.75
1.61
1.60
1.59
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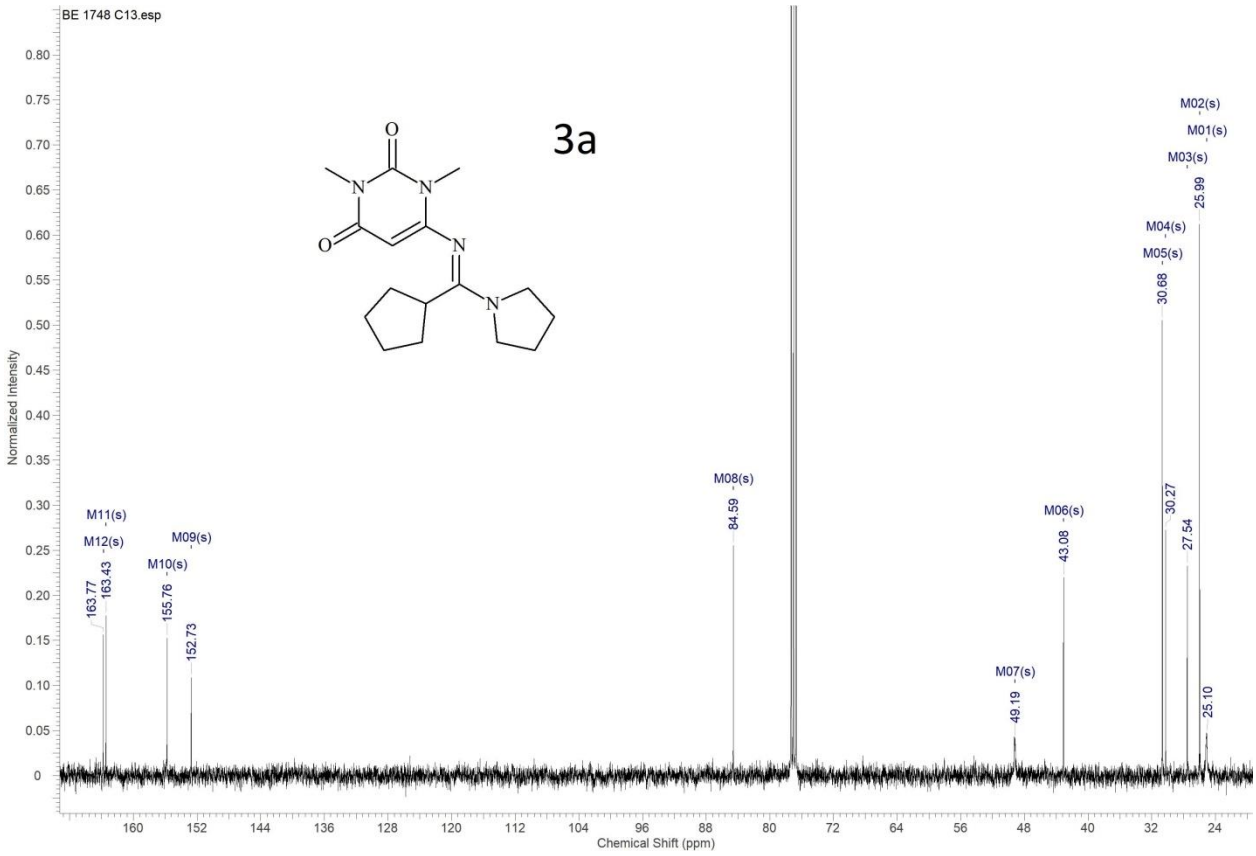
Chemical Shift (ppm)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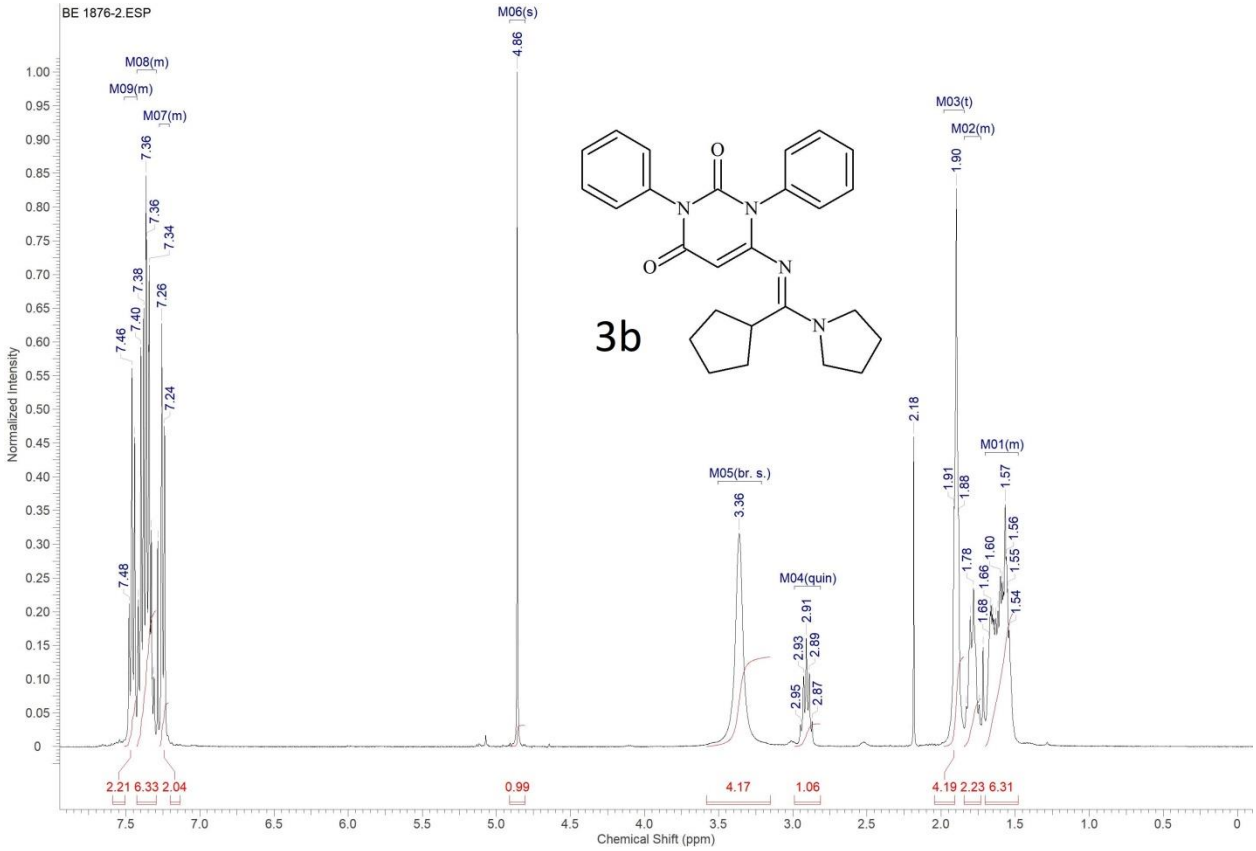
Normalized Intensity
Chemical Shift (ppm)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2.18
M01(m)
1.91
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1.57
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1.56
1.55
1.66
1.68
1.54
M05(br. s.)
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M04(quin)
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2.93
2.89
2.95
2.87
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Normalized Intensity
Chemical Shift (ppm)
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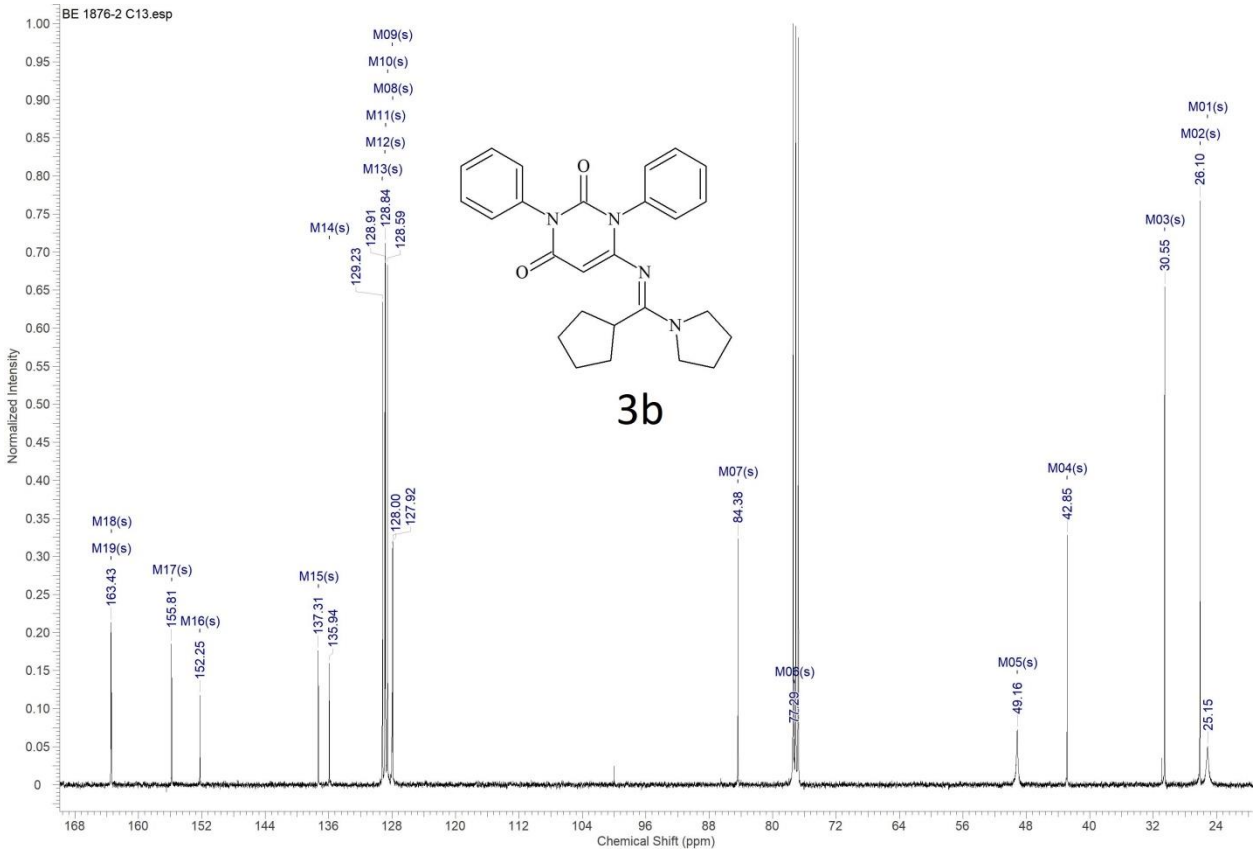
1.06
4.19 2.23 6.31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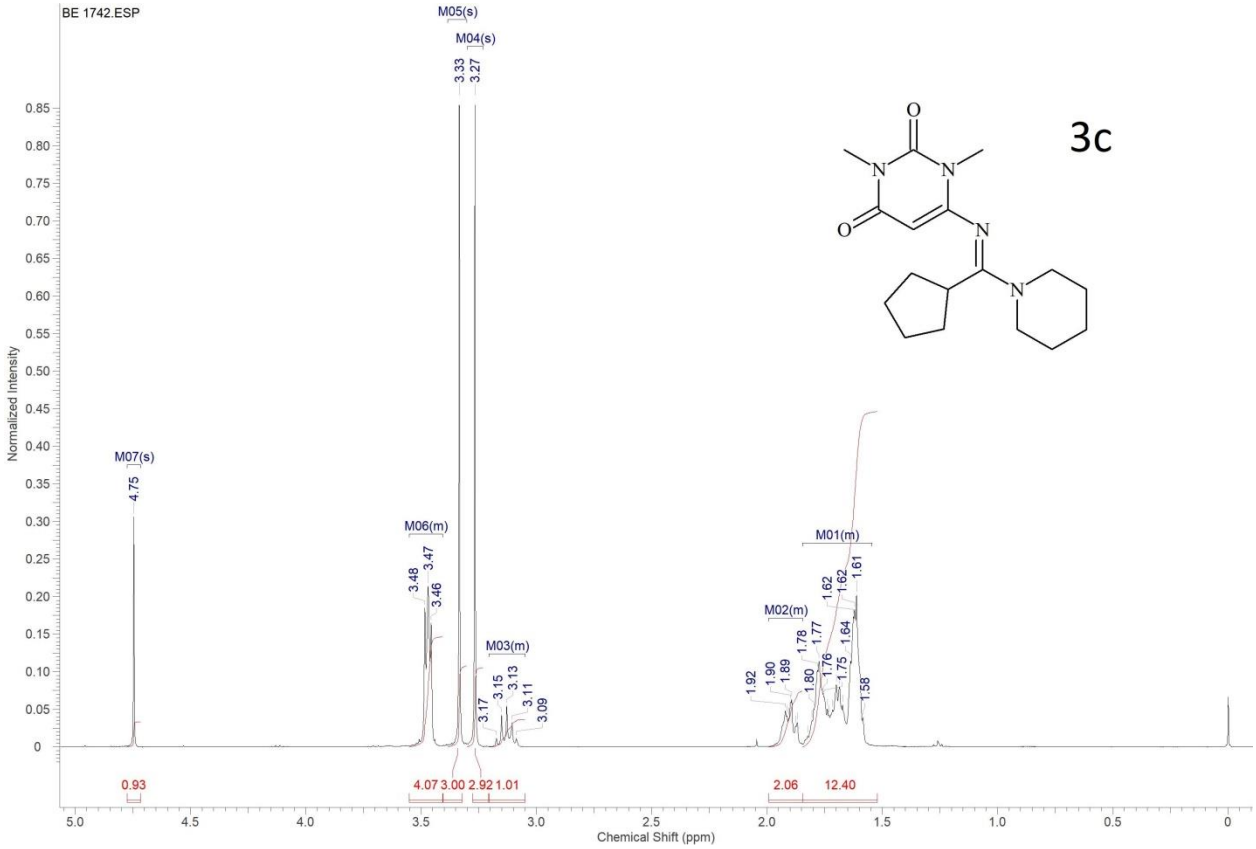
Normalized Intensity
Chemical Shift (ppm)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3.09
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1.80
M02(m)
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1.62
1.62
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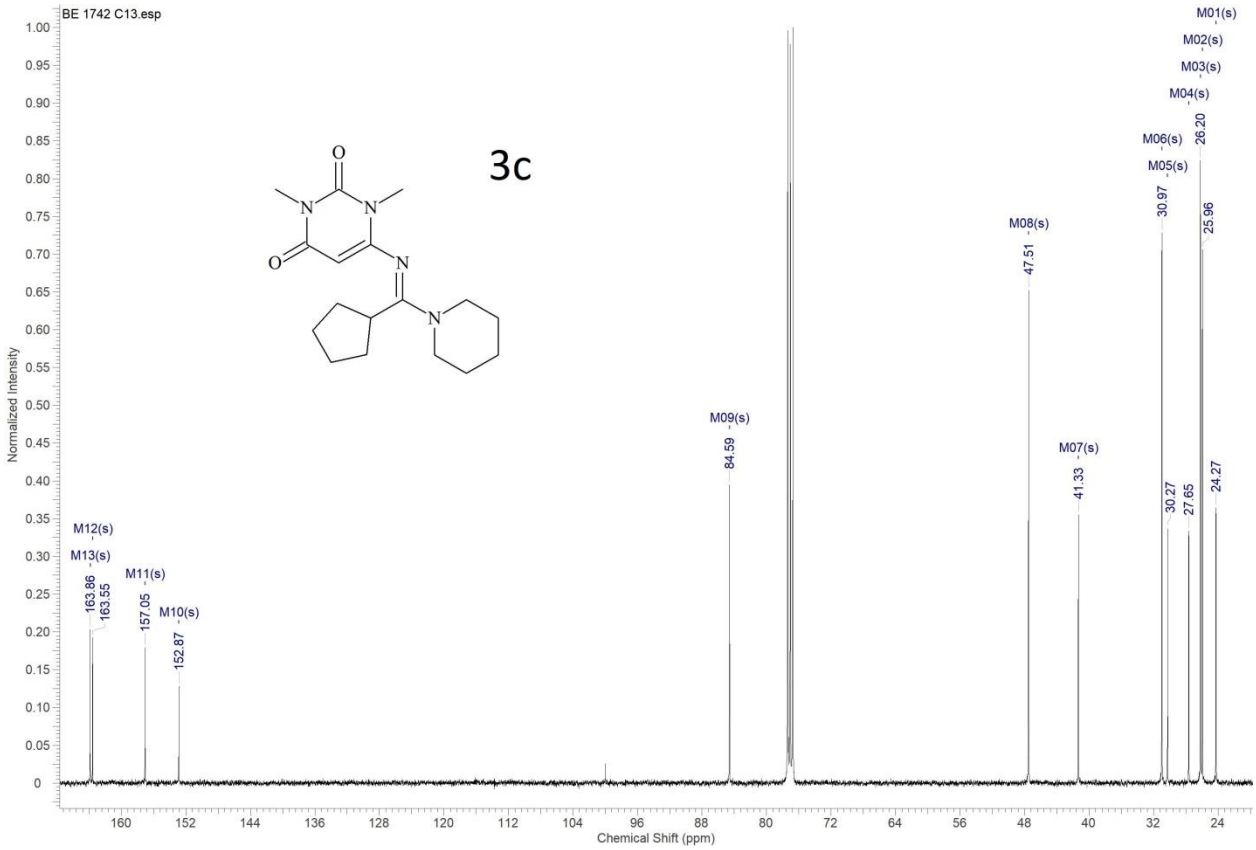
Normalized Intensity
Chemical Shift (ppm)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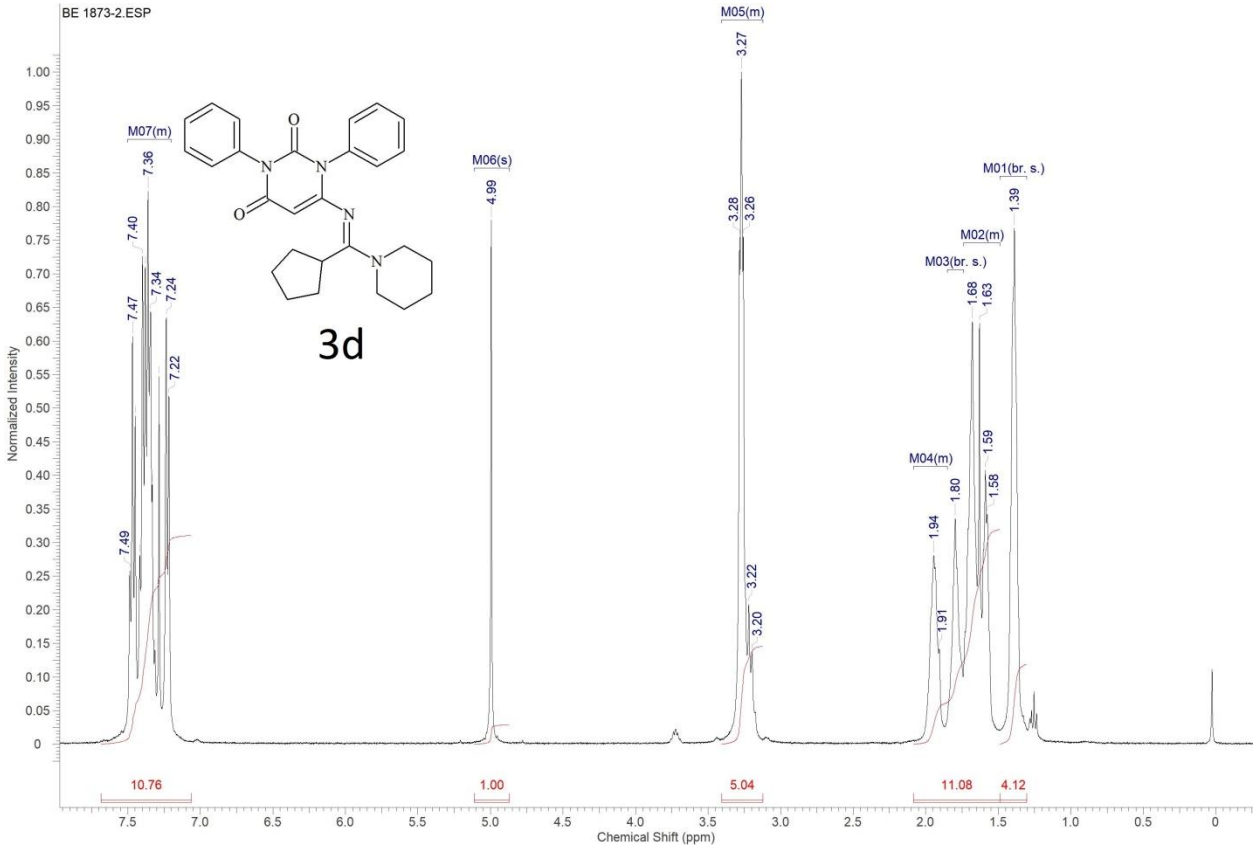
Normalized Intensity
Chemical Shift (ppm)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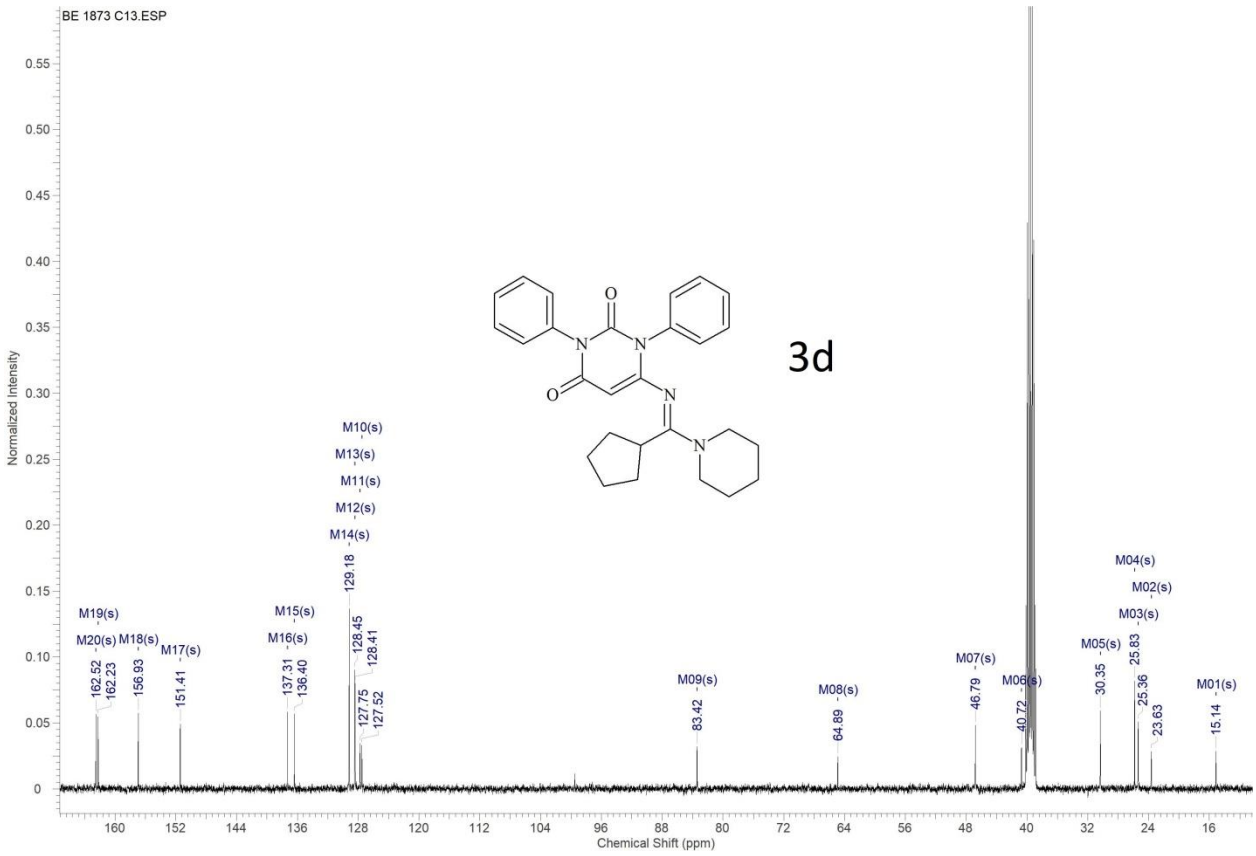
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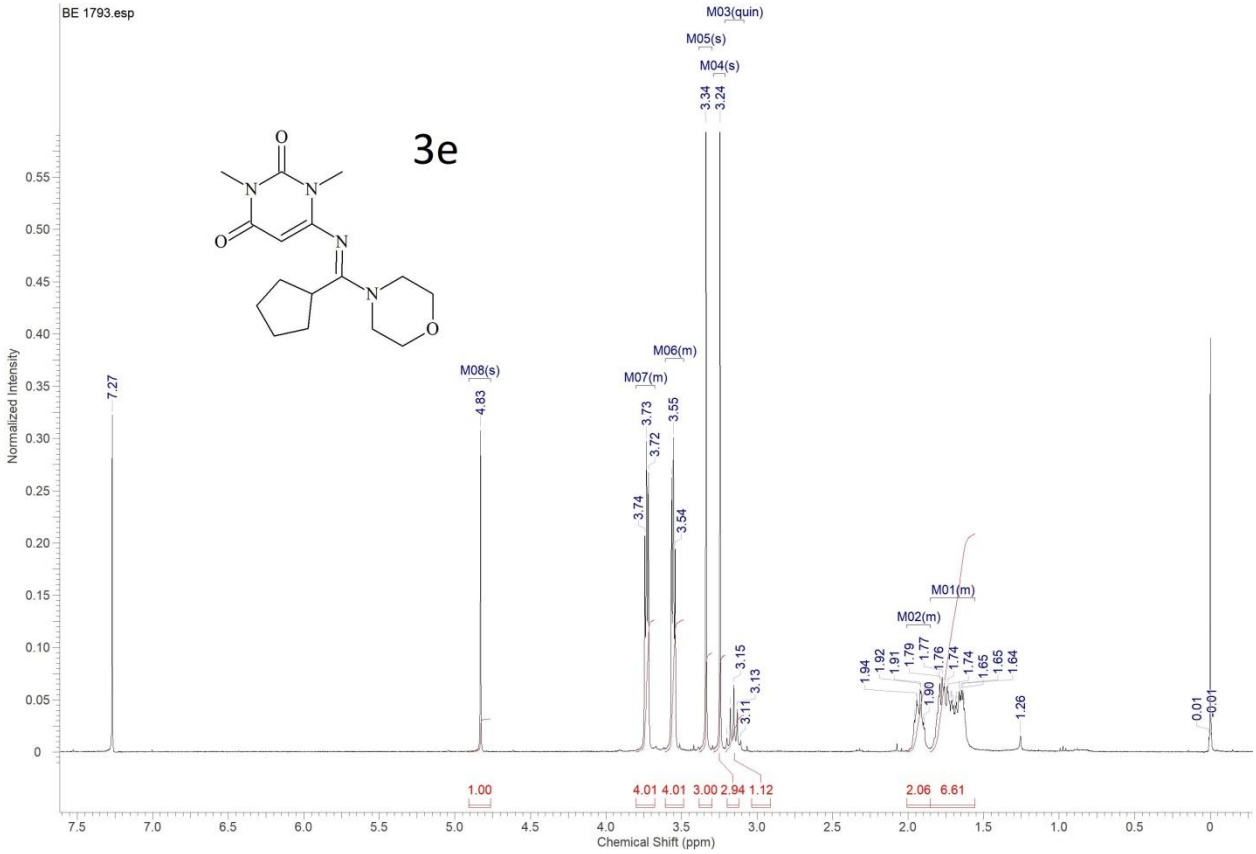
Normalized Intensity
Chemical Shift (ppm)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1.76
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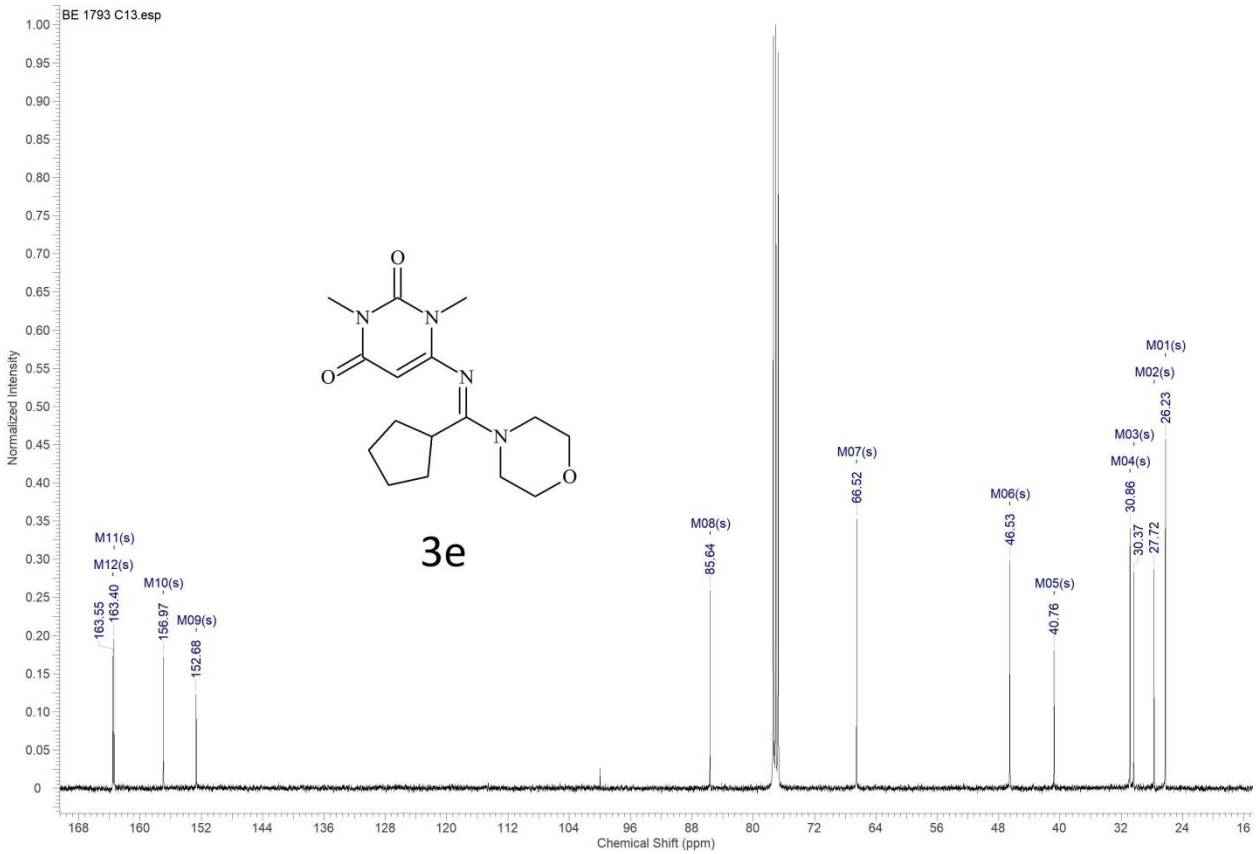
Normalized Intensity
Chemical Shift (ppm)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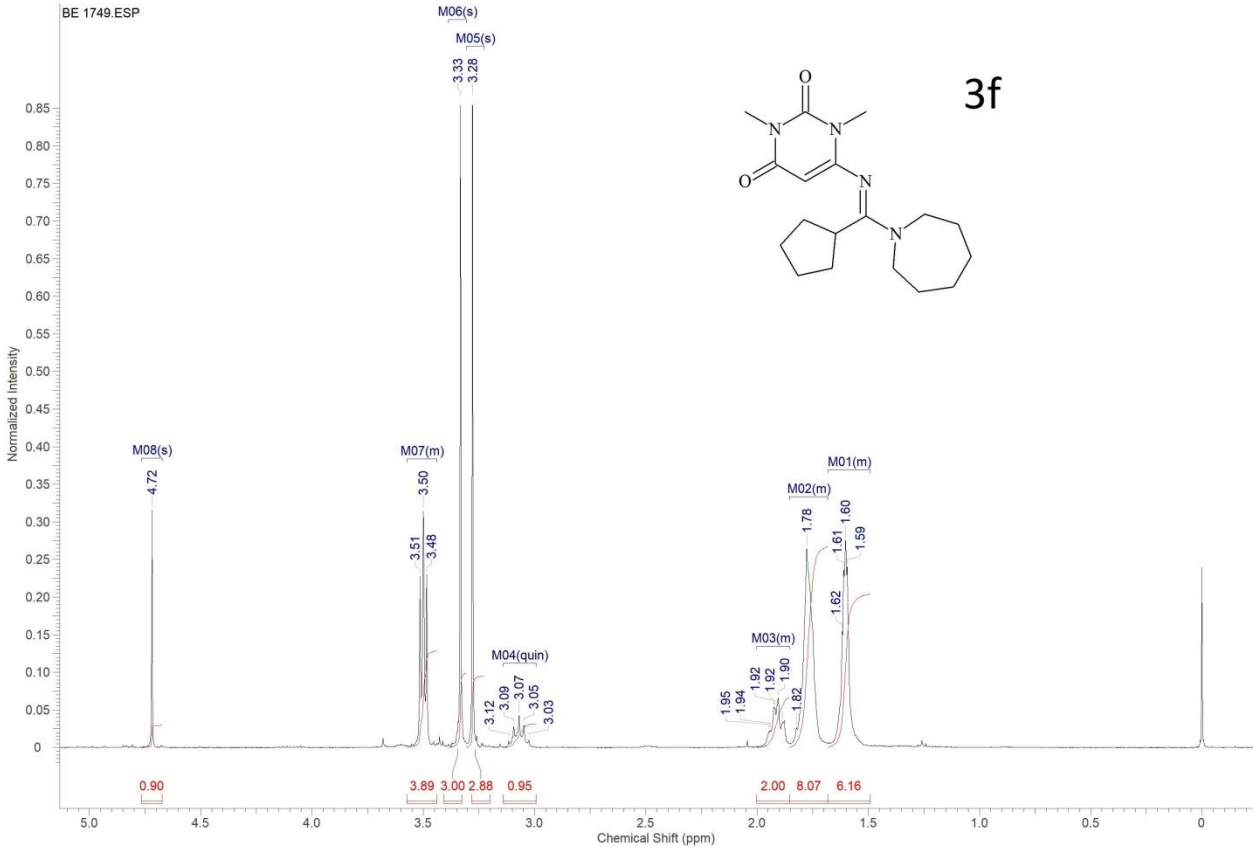
Normalized Intensity
Chemical Shift (ppm)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M02(m)
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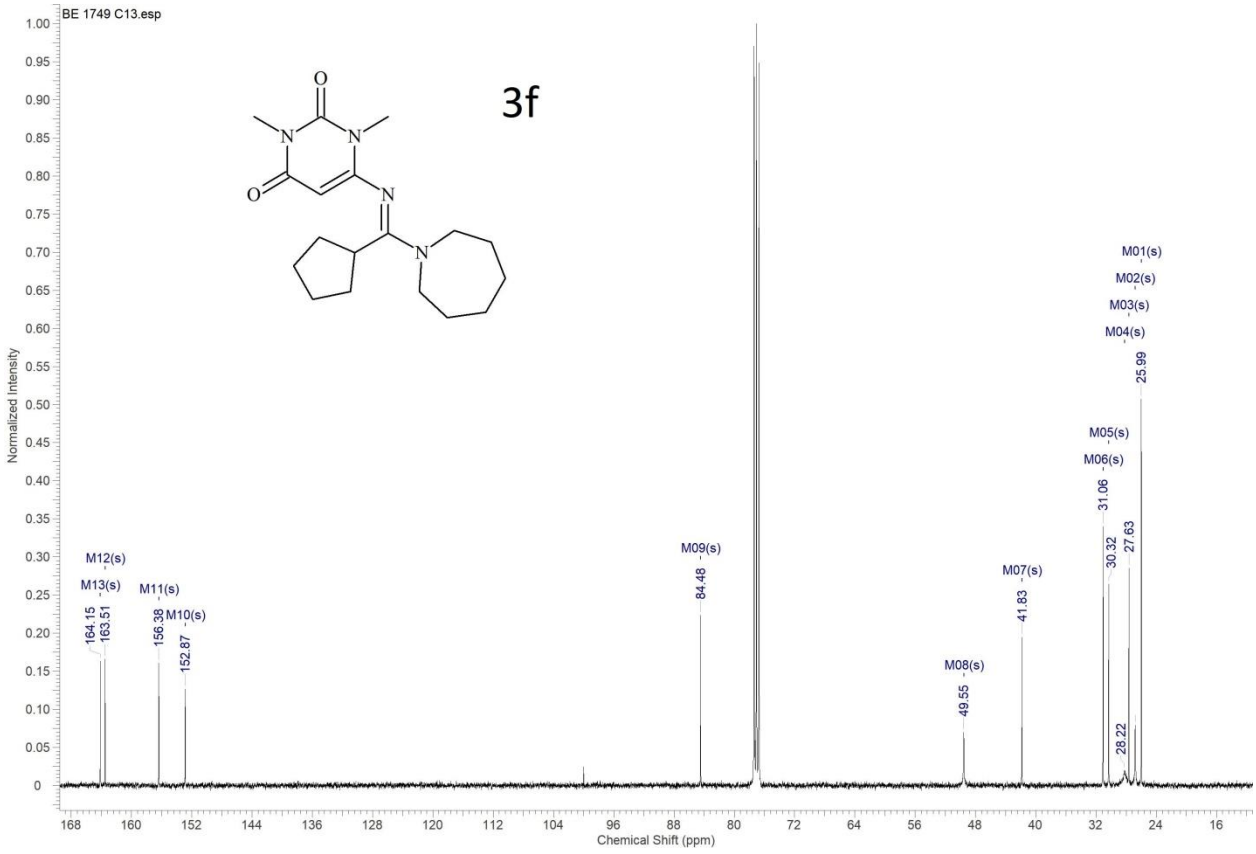
Chemical Shift (ppm)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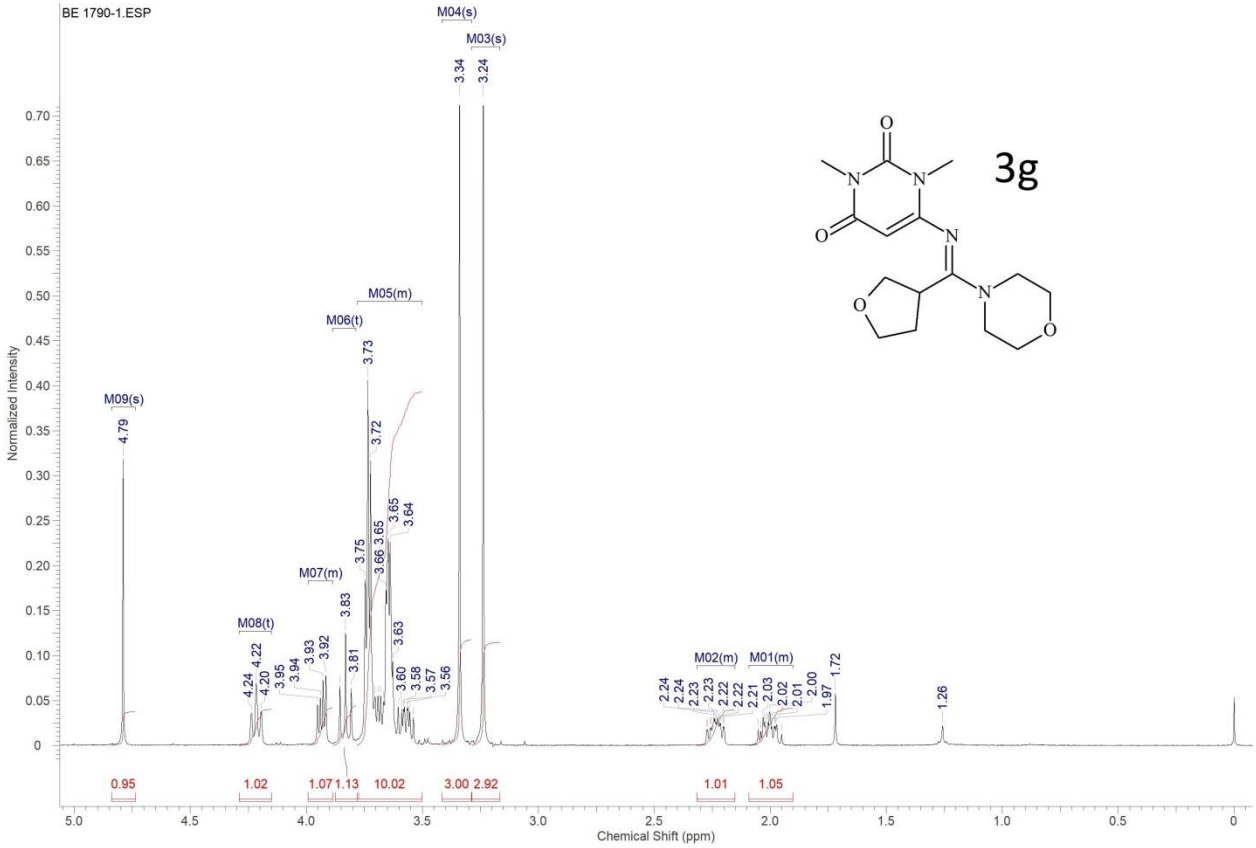
Normalized Intensity
Chemical Shift (ppm)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M08(t)
M02(m)
M01(m)
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3.24
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3.72
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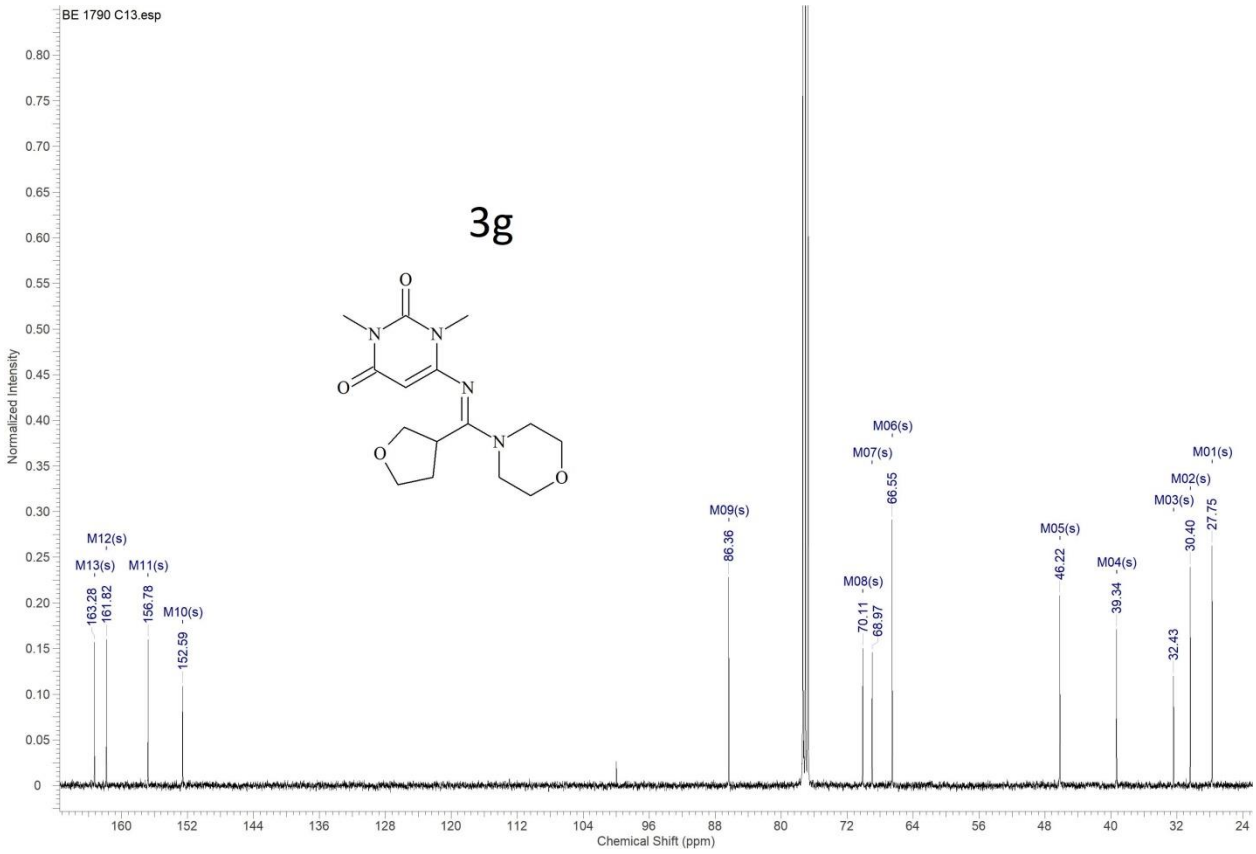
1.01
1.05


BE 1790 C13.esp
3g
Normalized Intensity
Chemical Shift (ppm)
M12(s)
M13(s)
M11(s)
M10(s)
M09(s)
M06(s)
M07(s)
M08(s)
M05(s)
M04(s)
M03(s)
M02(s)
M01(s)
163.28
161.82
156.78
152.59
86.36
66.55
70.11
68.97
46.22
39.34
32.43
30.40
27.75