

Design, Synthesis, Anti-Varicella-Zoster, and Antimicrobial Activity of (Isoxazolidin-3-yl)Phosphonate Conjugates of N1-Functionalised Quinazoline-2,4-Diones

Magdalena Łysakowska ¹, Iwona E. Głowacka ¹, Graciela Andrei ², Dominique Schols ², Robert Snoeck ², Paweł Lisiecki ³, Magdalena Szemraj ³ and Dorota G. Piotrowska ^{1,*}

¹. Bioorganic Chemistry Laboratory, Faculty of Pharmacy, Medical University of Lodz, Muszynskiego 1, 90-151 Lodz, Poland; magdalena.lysakowska@umed.lodz.pl (M.Ł.); iwona.glowacka@umed.lodz.pl (I.E.G.)

². KU Leuven Department of Microbiology, Immunology and Transplantation, Rega Institute, Laboratory of Virology and Chemotherapy, Herestraat 49, box 1030, B-3000 Leuven, Belgium; graciela.andrei@kuleuven.be (G.A.); dominique.schols@kuleuven.be (D.S.); robert.snoeck@kuleuven.be (R.S.);

³. Department of Pharmaceutical Microbiology and Microbiological Diagnostics, Faculty of Pharmacy, Medical University of Lodz, Muszynskiego 1, 90-151 Łódź, Poland; pawel.lisiecki@umed.lodz.pl (P.L.); magdalena.szemraj@umed.lodz.pl (M.S.)

* Correspondence: dorota.piotrowska@umed.lodz.pl (D.G.P.)

Contents

Figure S1: ¹H NMR Spectrum for *trans*-**20a** in CDCl₃

Figure S2: ³¹P NMR Spectrum for *trans*-**20a** in CDCl₃

Figure S3: ¹³C NMR Spectrum for *trans*-**20a** in CDCl₃

Figure S4: ¹H NMR Spectrum for *trans*-**20b** in CDCl₃

Figure S5: ³¹P NMR Spectrum for *trans*-**20b** in CDCl₃

Figure S6: ¹³C NMR Spectrum for *trans*-**20b** in CDCl₃

Figure S7: ¹H NMR Spectrum for *trans*-**20c** in CDCl₃

Figure S8: ³¹P NMR Spectrum for *trans*-**20c** in CDCl₃

Figure S9: ¹³C NMR Spectrum for *trans*-**20c** in CDCl₃

Figure S10: ¹H NMR Spectrum for *trans*-**20d** in CDCl₃

Figure S11: ³¹P NMR Spectrum for *trans*-**20d** in CDCl₃

Figure S12: ¹³C NMR Spectrum for *trans*-**20d** in CDCl₃

Figure S13: ¹H NMR Spectrum for *trans*-**21a** in CDCl₃

Figure S14: ^{31}P NMR Spectrum for *trans*-**21a** in CDCl_3

Figure S15: ^{13}C NMR Spectrum for *trans*-**21a** in CDCl_3

Figure S16: ^1H NMR Spectrum for *trans*-**21b** in CDCl_3

Figure S17: ^{31}P NMR Spectrum for *trans*-**21b** in CDCl_3

Figure S18: ^{13}C NMR Spectrum for *trans*-**21b** in CDCl_3

Figure S19: ^1H NMR Spectrum for *trans*-**21c** in CDCl_3

Figure S20: ^{31}P NMR Spectrum for *trans*-**21c** in CDCl_3

Figure S21: ^{13}C NMR Spectrum for *trans*-**21c** in CDCl_3

Figure S22: ^1H NMR Spectrum for *trans*-**21d** in CDCl_3

Figure S23: ^{31}P NMR Spectrum for *trans*-**21d** in CDCl_3

Figure S24: ^{13}C NMR Spectrum for *trans*-**21d** in CDCl_3

Figure S25: ^1H NMR Spectrum for **24a** in CDCl_3

Figure S26: ^{13}C NMR Spectrum for **24a** in CDCl_3

Figure S27: ^1H NMR Spectrum for **24b** in CDCl_3

Figure S28: ^{13}C NMR Spectrum for **24b** in CDCl_3

Figure S29: ^1H NMR Spectrum for **24c** in CDCl_3

Figure S30: ^{13}C NMR Spectrum for **24c** in CDCl_3

Figure S31: ^1H NMR Spectrum for **24d** in CDCl_3

Figure S32: ^{13}C NMR Spectrum for **24d** in CDCl_3

Figure S33: ^1H NMR Spectrum for **26a** in CDCl_3

Figure S34: ^{13}C NMR Spectrum for **26a** in CDCl_3

Figure S35: ^1H NMR Spectrum for **26b** in CDCl_3

Figure S36: ^{13}C NMR Spectrum for **26b** in CDCl_3

Figure S37: ^1H NMR Spectrum for **26c** in CDCl_3

Figure S38: ^{13}C NMR Spectrum for **26c** in CDCl_3

Figure S39: ^1H NMR Spectrum for **26d** in CDCl_3

Figure S40: ^{13}C NMR Spectrum for **26d** in CDCl_3

Figure S41: ^1H NMR Spectrum for **27a** in CDCl_3

Figure S42: ^{13}C NMR Spectrum for **27a** in CDCl_3

Figure S43: ^1H NMR Spectrum for **27b** in CDCl_3

Figure S44: ^{13}C NMR Spectrum for **27b** in CDCl_3

Figure S45: ^1H NMR Spectrum for **27c** in CDCl_3

Figure S46: ^{13}C NMR Spectrum for **27c** in CDCl_3

Figure S47: ^1H NMR Spectrum for **27d** in CDCl_3

Figure S48: ^{13}C NMR Spectrum for **27d** in CDCl_3

Figure S1: ^1H NMR Spectrum for *trans*-**20a** in CDCl_3

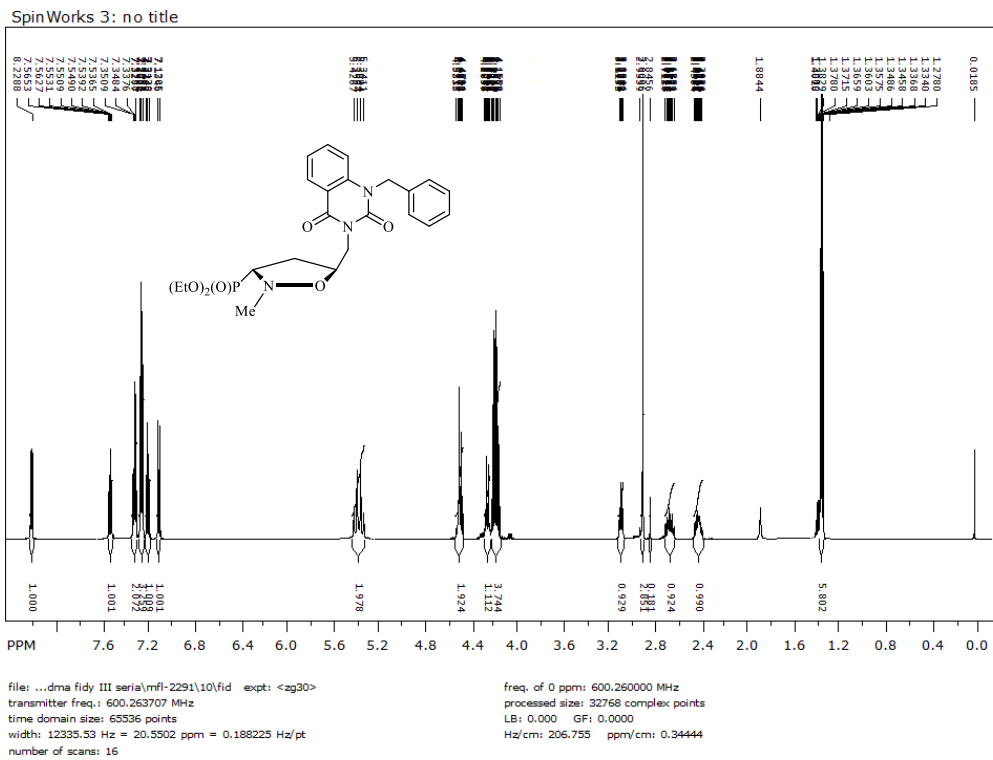


Figure S2: ^{31}P NMR Spectrum for *trans*-**20a** in CDCl_3

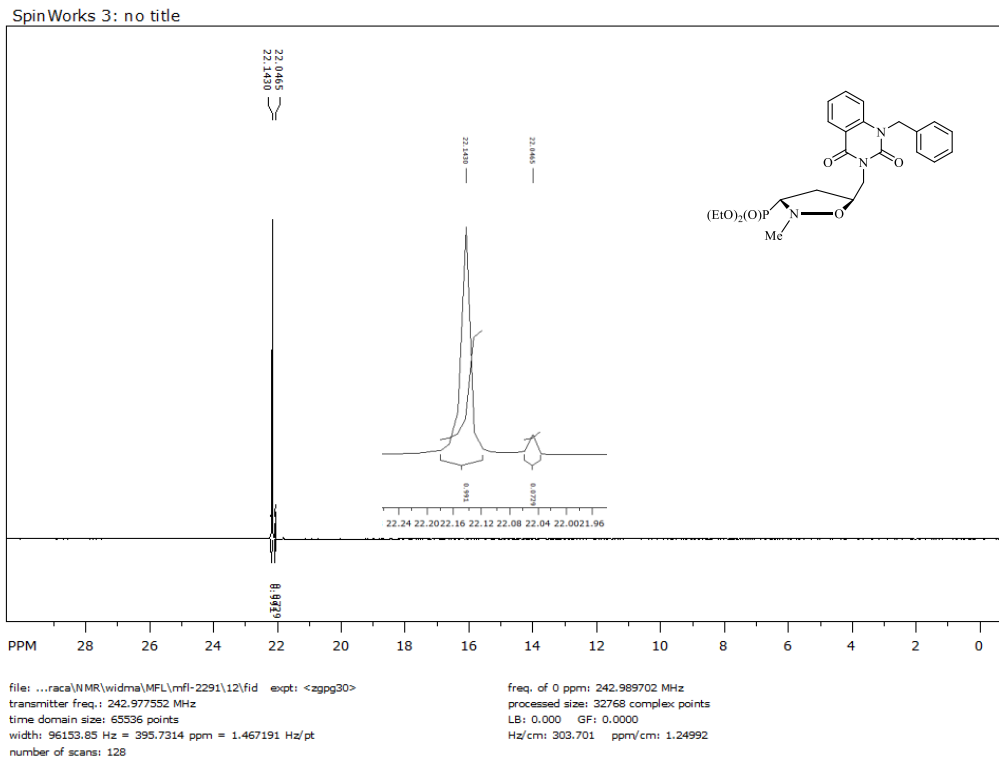


Figure S3: ^{13}C NMR Spectrum for *trans*-**20a** in CDCl_3

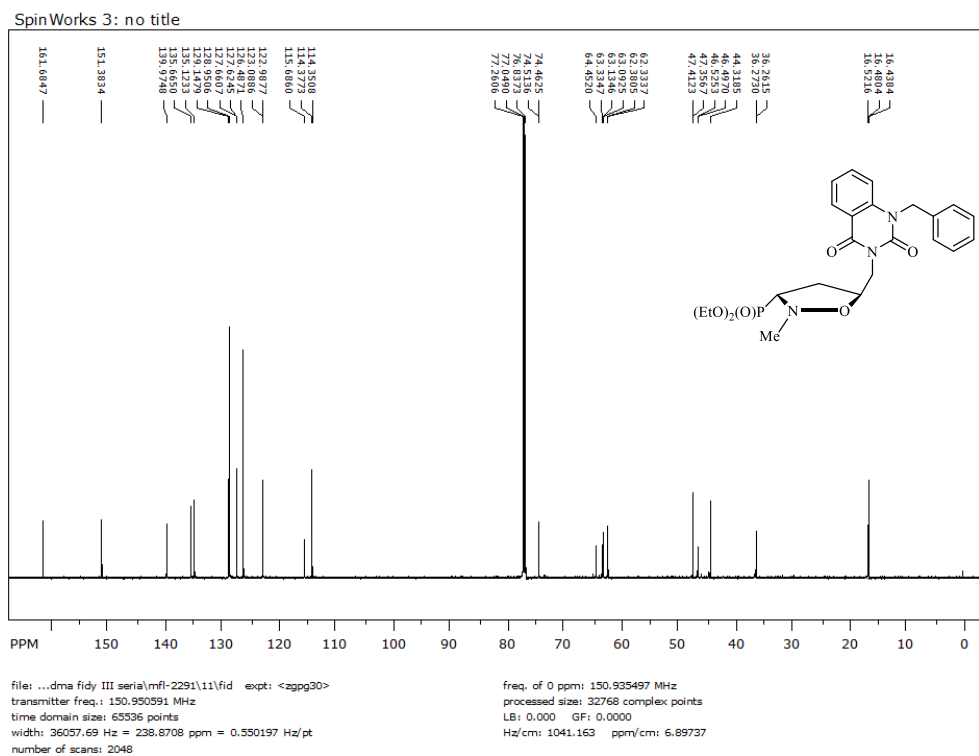


Figure S4: ^1H NMR Spectrum for *trans*-**20b** in CDCl_3

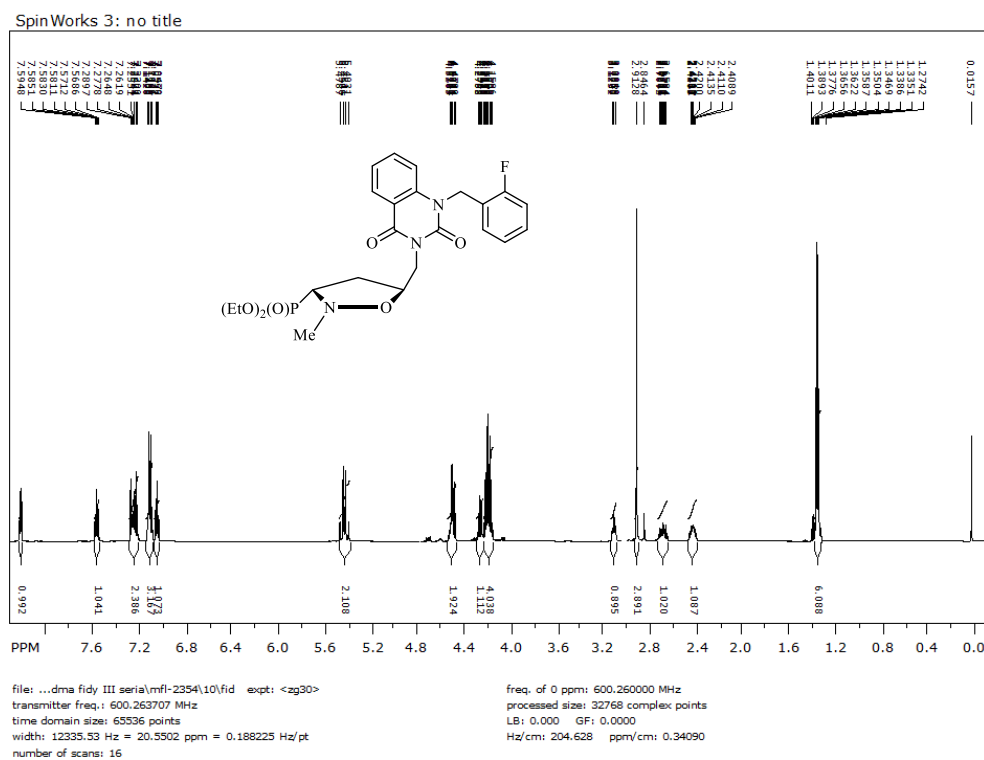


Figure S5: ^{31}P NMR Spectrum for *trans*-**20b** in CDCl_3

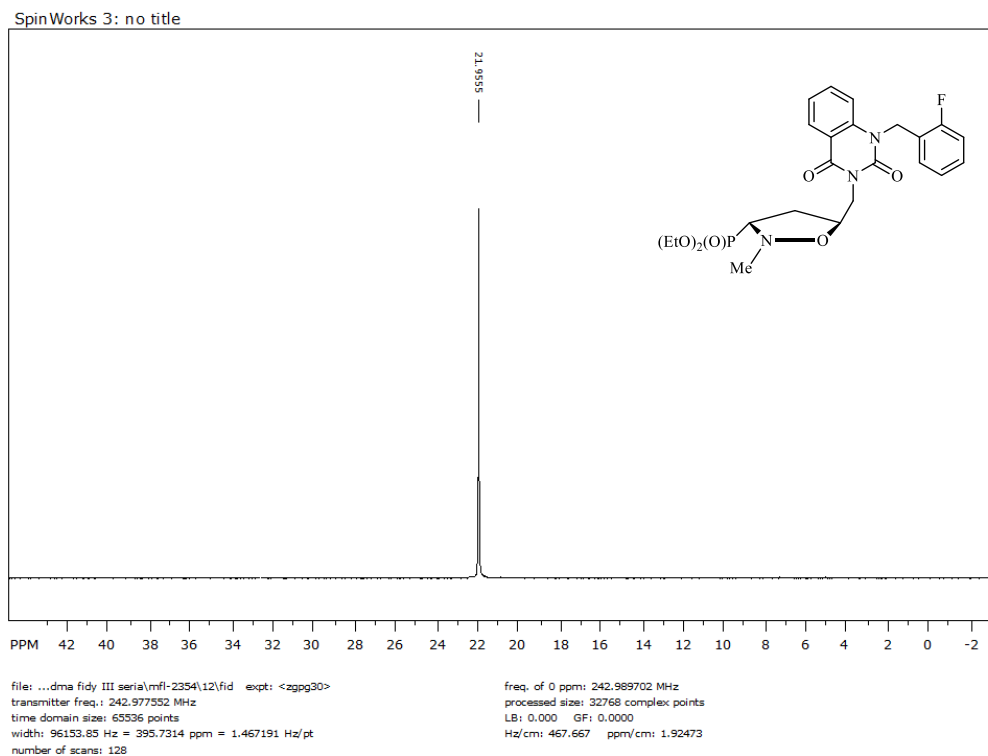


Figure S6: ^{13}C NMR Spectrum for *trans*-**20b** in CDCl_3

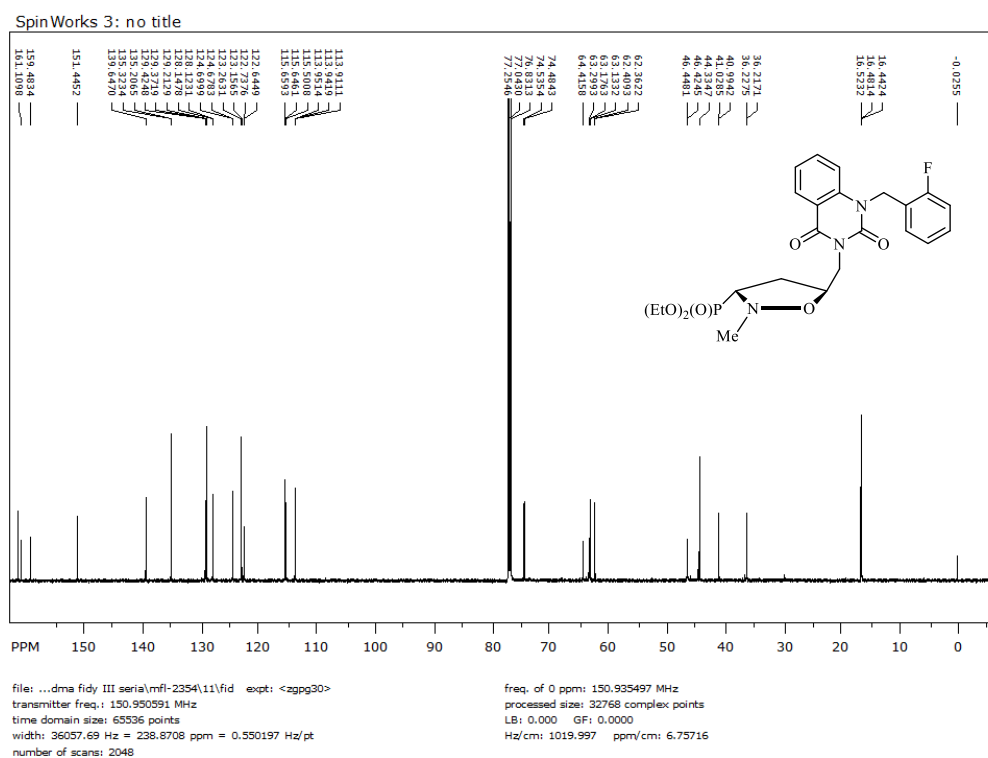


Figure S7: ^1H NMR Spectrum for *trans*-**20c** in CDCl_3

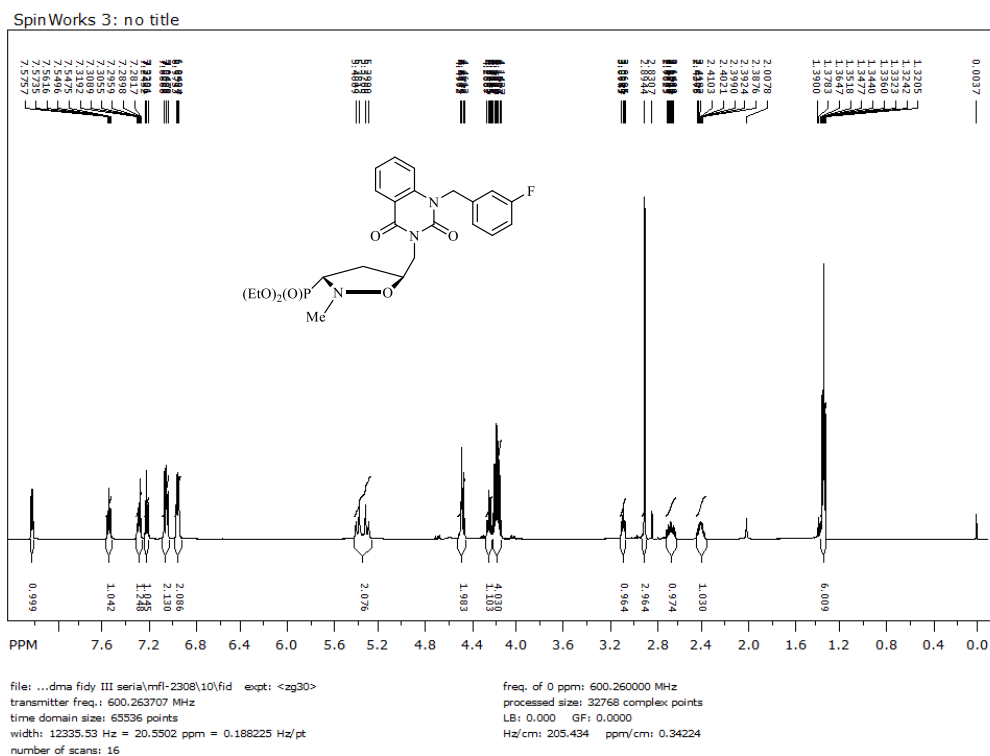


Figure S8: ^{31}P NMR Spectrum for *trans*-**20c** in CDCl_3

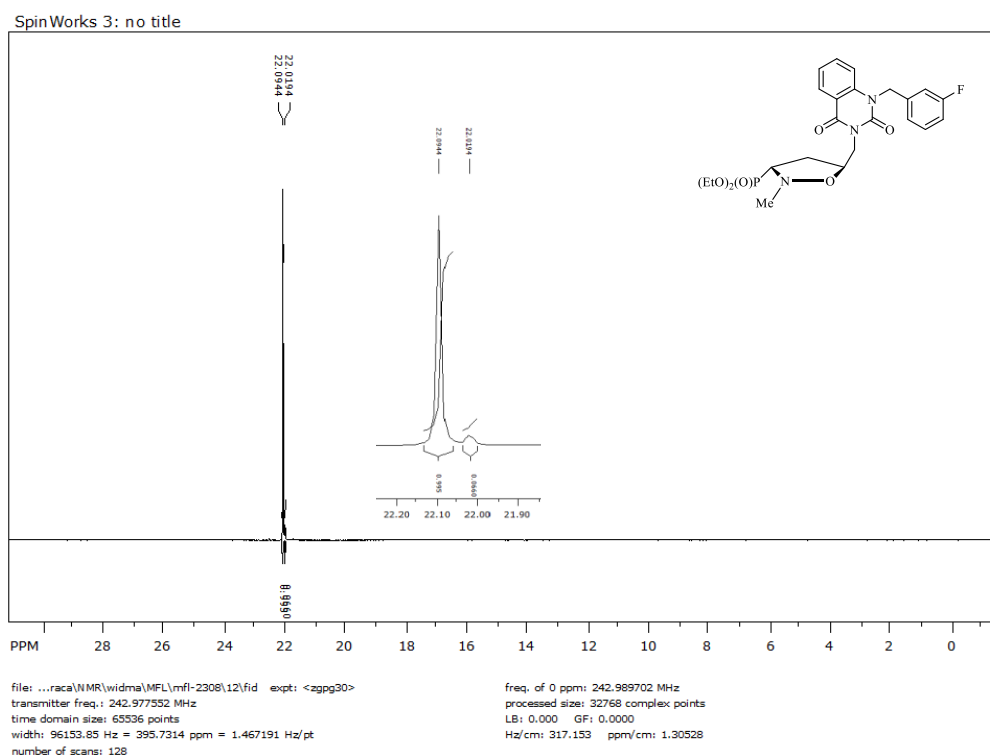


Figure S9: ^{13}C NMR Spectrum for *trans*-**20c** in CDCl_3

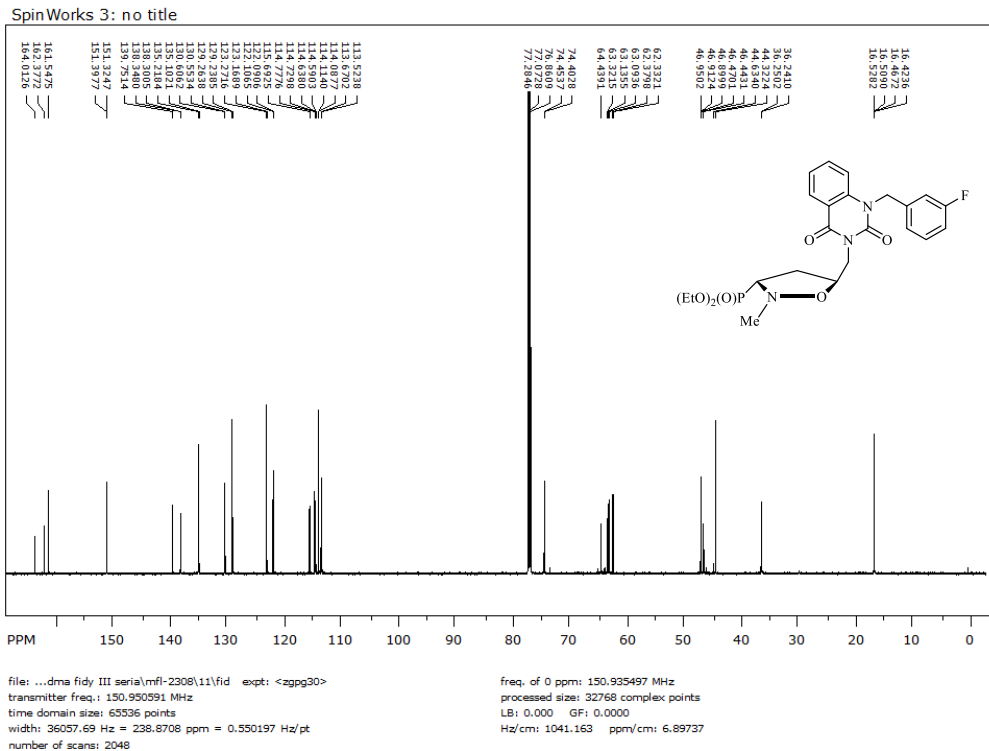


Figure S10: ^1H NMR Spectrum for *trans*-**20d** in CDCl_3

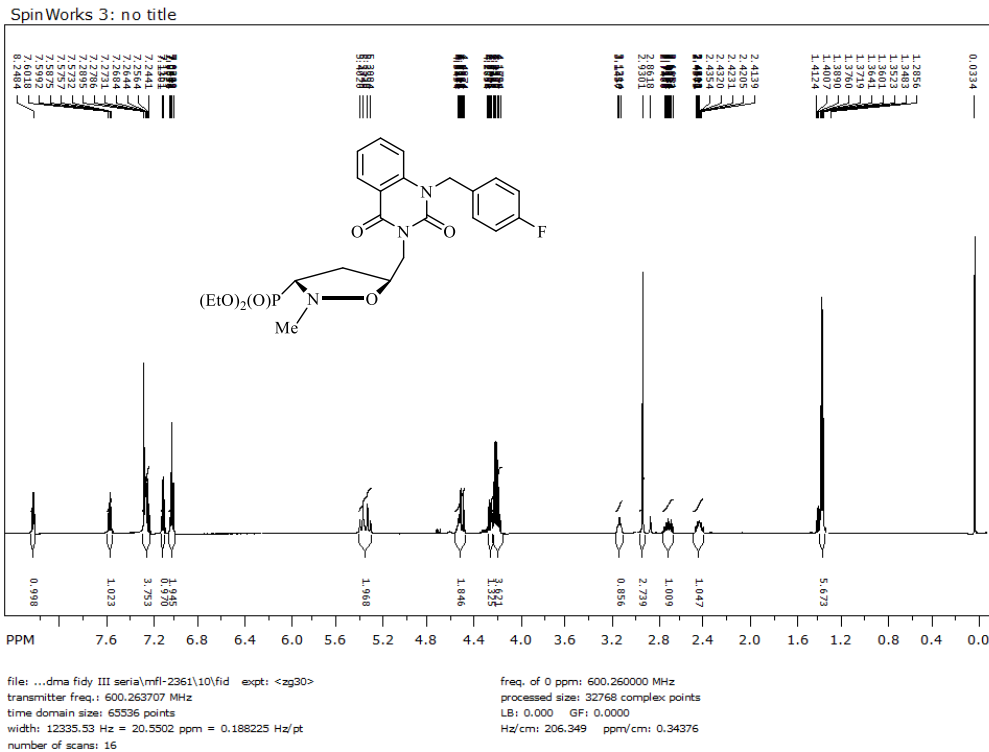


Figure S11: ^{31}P NMR Spectrum for *trans*-20d in CDCl_3

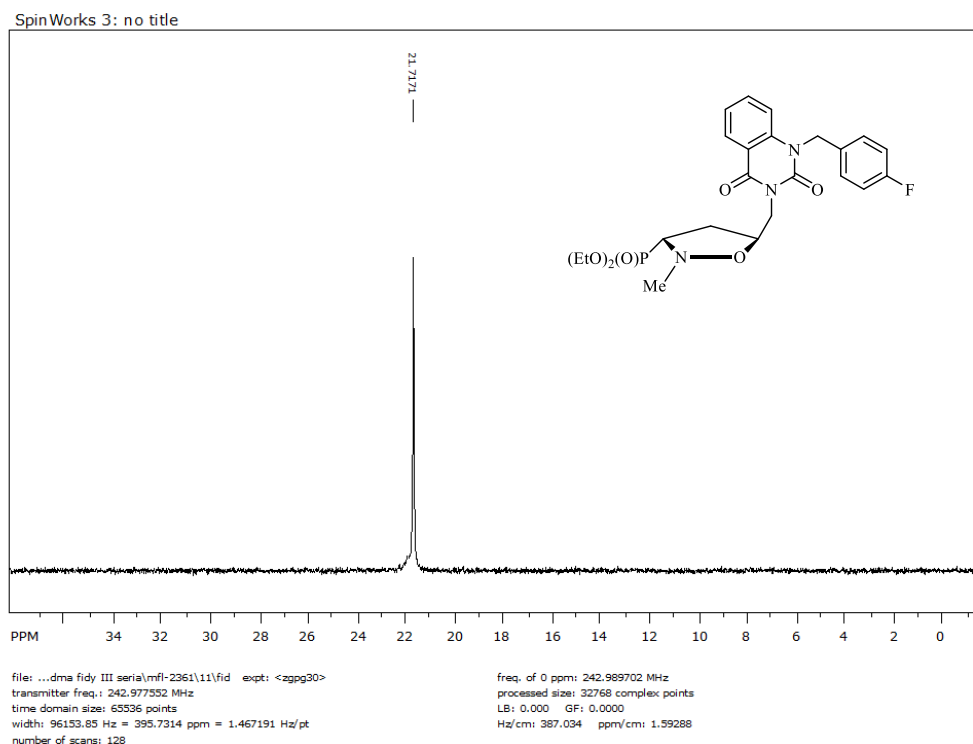
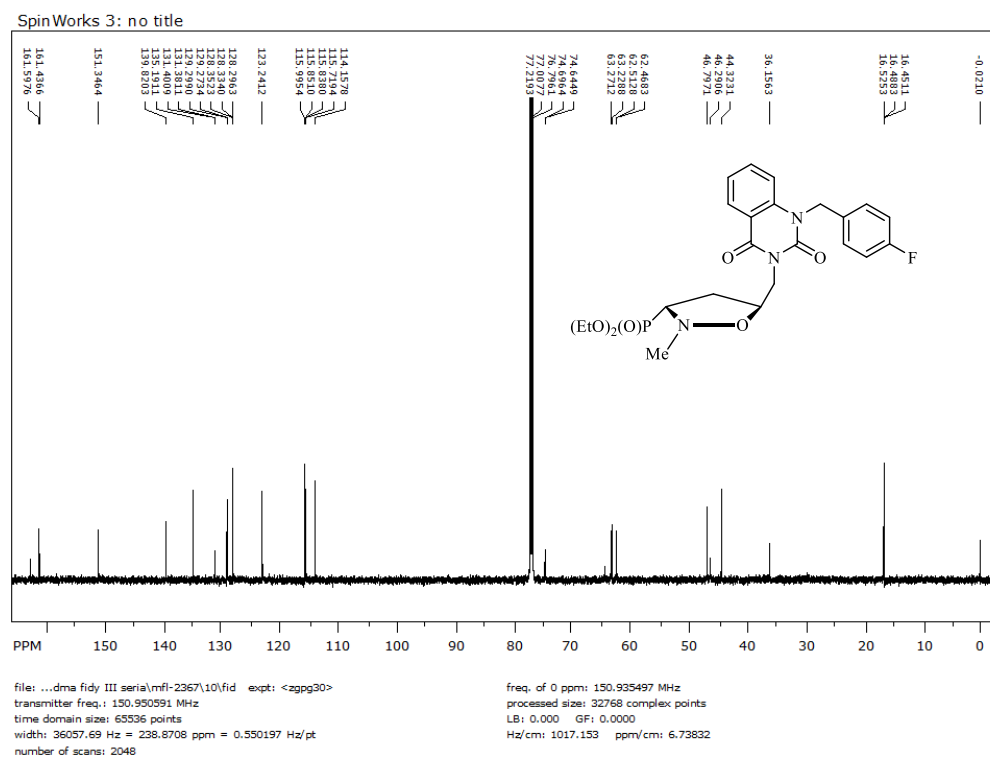


Figure S12: ^{13}C NMR Spectrum for *trans*-20d in CDCl_3



SpinWorks 3: no title

Chemical structure: CCOP(=O)(OCC)N1CCOC1CN2C(=O)c3ccccc3C2=O

Integration values (from left to right): 1.000, 1.017, 1.065, 2.066, 2.196, 2.240, 1.018, 2.308, 3.422, 1.061, 1.021, 1.045, 1.069, 6.309.

Peak lists (from left to right):

- 7.998, 7.994, 7.990, 7.986, 7.982, 7.978, 7.974, 7.970, 7.966, 7.962, 7.958, 7.954, 7.950, 7.946, 7.942, 7.938, 7.934, 7.930, 7.926, 7.922, 7.918, 7.914, 7.910, 7.906, 7.902, 7.898, 7.894, 7.890, 7.886, 7.882, 7.878, 7.874, 7.870, 7.866, 7.862, 7.858, 7.854, 7.850, 7.846, 7.842, 7.838, 7.834, 7.830, 7.826, 7.822, 7.818, 7.814, 7.810, 7.806, 7.802, 7.798, 7.794, 7.790, 7.786, 7.782, 7.778, 7.774, 7.770, 7.766, 7.762, 7.758, 7.754, 7.750, 7.746, 7.742, 7.738, 7.734, 7.730, 7.726, 7.722, 7.718, 7.714, 7.710, 7.706, 7.702, 7.698, 7.694, 7.690, 7.686, 7.682, 7.678, 7.674, 7.670, 7.666, 7.662, 7.658, 7.654, 7.650, 7.646, 7.642, 7.638, 7.634, 7.630, 7.626, 7.622, 7.618, 7.614, 7.610, 7.606, 7.602, 7.598, 7.594, 7.590, 7.586, 7.582, 7.578, 7.574, 7.570, 7.566, 7.562, 7.558, 7.554, 7.550, 7.546, 7.542, 7.538, 7.534, 7.530, 7.526, 7.522, 7.518, 7.514, 7.510, 7.506, 7.502, 7.498, 7.494, 7.490, 7.486, 7.482, 7.478, 7.474, 7.470, 7.466, 7.462, 7.458, 7.454, 7.450, 7.446, 7.442, 7.438, 7.434, 7.430, 7.426, 7.422, 7.418, 7.414, 7.410, 7.406, 7.402, 7.398, 7.394, 7.390, 7.386, 7.382, 7.378, 7.374, 7.370, 7.366, 7.362, 7.358, 7.354, 7.350, 7.346, 7.342, 7.338, 7.334, 7.330, 7.326, 7.322, 7.318, 7.314, 7.310, 7.306, 7.302, 7.298, 7.294, 7.290, 7.286, 7.282, 7.278, 7.274, 7.270, 7.266, 7.262, 7.258, 7.254, 7.250, 7.246, 7.242, 7.238, 7.234, 7.230, 7.226, 7.222, 7.218, 7.214, 7.210, 7.206, 7.202, 7.198, 7.194, 7.190, 7.186, 7.182, 7.178, 7.174, 7.170, 7.166, 7.162, 7.158, 7.154, 7.150, 7.146, 7.142, 7.138, 7.134, 7.130, 7.126, 7.122, 7.118, 7.114, 7.110, 7.106, 7.102, 7.098, 7.094, 7.090, 7.086, 7.082, 7.078, 7.074, 7.070, 7.066, 7.062, 7.058, 7.054, 7.050, 7.046, 7.042, 7.038, 7.034, 7.030, 7.026, 7.022, 7.018, 7.014, 7.010, 7.006, 7.002, 6.998, 6.994, 6.990, 6.986, 6.982, 6.978, 6.974, 6.970, 6.966, 6.962, 6.958, 6.954, 6.950, 6.946, 6.942, 6.938, 6.934, 6.930, 6.926, 6.922, 6.918, 6.914, 6.910, 6.906, 6.902, 6.898, 6.894, 6.890, 6.886, 6.882, 6.878, 6.874, 6.870, 6.866, 6.862, 6.858, 6.854, 6.850, 6.846, 6.842, 6.838, 6.834, 6.830, 6.826, 6.822, 6.818, 6.814, 6.810, 6.806, 6.802, 6.798, 6.794, 6.790, 6.786, 6.782, 6.778, 6.774, 6.770, 6.766, 6.762, 6.758, 6.754, 6.750, 6.746, 6.742, 6.738, 6.734, 6.730, 6.726, 6.722, 6.718, 6.714, 6.710, 6.706, 6.702, 6.698, 6.694, 6.690, 6.686, 6.682, 6.678, 6.674, 6.670, 6.666, 6.662, 6.658, 6.654, 6.650, 6.646, 6.642, 6.638, 6.634, 6.630, 6.626, 6.622, 6.618, 6.614, 6.610, 6.606, 6.602, 6.598, 6.594, 6.590, 6.586, 6.582, 6.578, 6.574, 6.570, 6.566, 6.562, 6.558, 6.554, 6.550, 6.546, 6.542, 6.538, 6.534, 6.530, 6.526, 6.522, 6.518, 6.514, 6.510, 6.506, 6.502, 6.498, 6.494, 6.490, 6.486, 6.482, 6.478, 6.474, 6.470, 6.466, 6.462, 6.458, 6.454, 6.450, 6.446, 6.442, 6.438, 6.434, 6.430, 6.426, 6.422, 6.418, 6.414, 6.410, 6.406, 6.402, 6.398, 6.394, 6.390, 6.386, 6.382, 6.378, 6.374, 6.370, 6.366, 6.362, 6.358, 6.354, 6.350, 6.346, 6.342, 6.338, 6.334, 6.330, 6.326, 6.322, 6.318, 6.314, 6.310, 6.306, 6.302, 6.298, 6.294, 6.290, 6.286, 6.282, 6.278, 6.274, 6.270, 6.266, 6.262, 6.258, 6.254, 6.250, 6.246, 6.242, 6.238, 6.234, 6.230, 6.226, 6.222, 6.218, 6.214, 6.210, 6.206, 6.202, 6.198, 6.194, 6.190, 6.186, 6.182, 6.178, 6.174, 6.170, 6.166, 6.162, 6.158, 6.154, 6.150, 6.146, 6.142, 6.138, 6.134, 6.130, 6.126, 6.122, 6.118, 6.114, 6.110, 6.106, 6.102, 6.098, 6.094, 6.090, 6.086, 6.082, 6.078, 6.074, 6.070, 6.066, 6.062, 6.058, 6.054, 6.050, 6.046, 6.042, 6.038, 6.034, 6.030, 6.026, 6.022, 6.018, 6.014, 6.010, 6.006, 6.002, 5.998, 5.994, 5.990, 5.986, 5.982, 5.978, 5.974, 5.970, 5.966, 5.962, 5.958, 5.954, 5.950, 5.946, 5.942, 5.938, 5.934, 5.930, 5.926, 5.922, 5.918, 5.914, 5.910, 5.906, 5.902, 5.898, 5.894, 5.890, 5.886, 5.882, 5.878, 5.874, 5.870, 5.866, 5.862, 5.858, 5.854, 5.850, 5.846, 5.842, 5.838, 5.834, 5.830, 5.826, 5.822, 5.818, 5.814, 5.810, 5.806, 5.802, 5.798,

SpinWorks 3: no title

Chemical structure of compound 10: CCOP(=O)(OCC)N1CCOC1CN2C(=O)c3ccccc3N2C(=O)c4ccccc4

¹H NMR spectrum (CDCl₃) showing peaks at 22.1786 ppm (integration 0.14) and 22.1290 ppm (integration 1.00).

File: ...dma.fid III serial(MFL-2269\12\fid exp: <zpgg30>
 transmitter freq.: 242.977552 MHz
 time domain size: 65536 points
 width: 96153.85 Hz = 395.7314 ppm = 1.467191 Hz/pt
 number of scans: 16

freq. of 0 ppm: 242.989702 MHz
 processed size: 32768 complex points
 LB: 1.000 GF: 0.0000
 Hz/cm: 334.904 ppm/cm: 1.37833

Figure S15: ^{13}C NMR Spectrum for *trans*-**21a** in CDCl_3

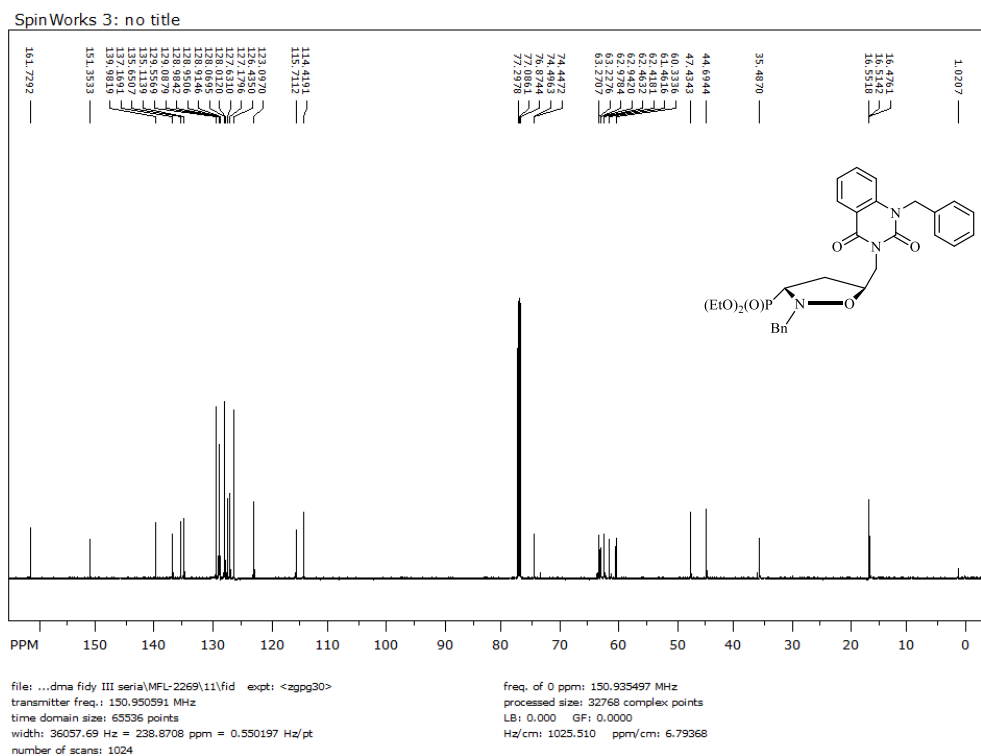


Figure S16: ^1H NMR Spectrum for *trans*-**21b** in CDCl_3

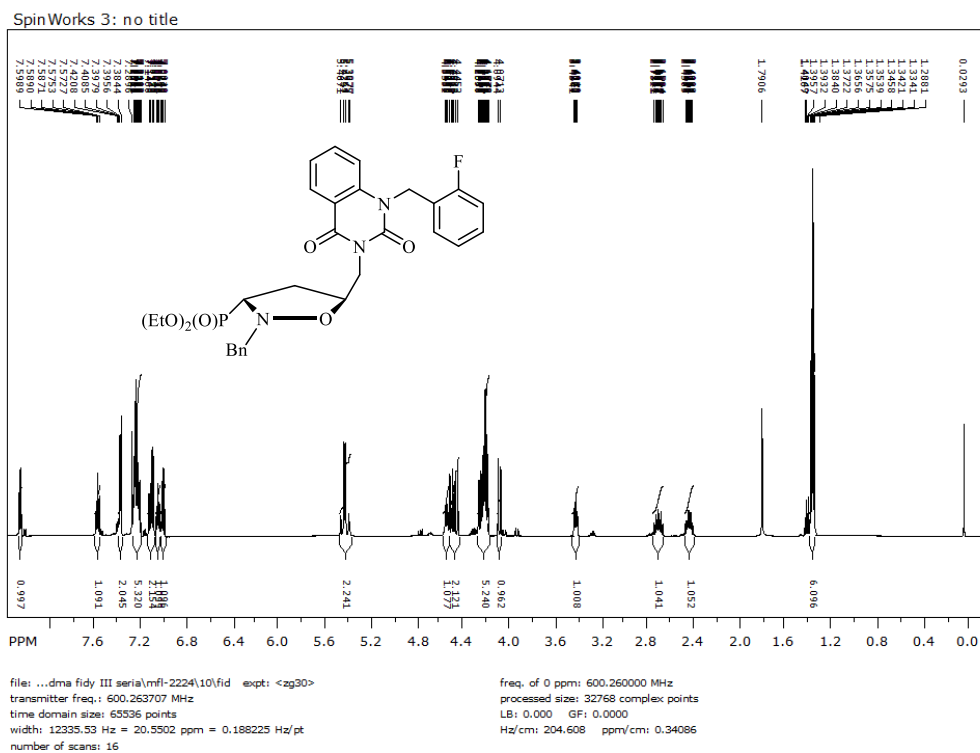


Figure S17: ^{31}P NMR Spectrum for *trans*-**21b** in CDCl_3

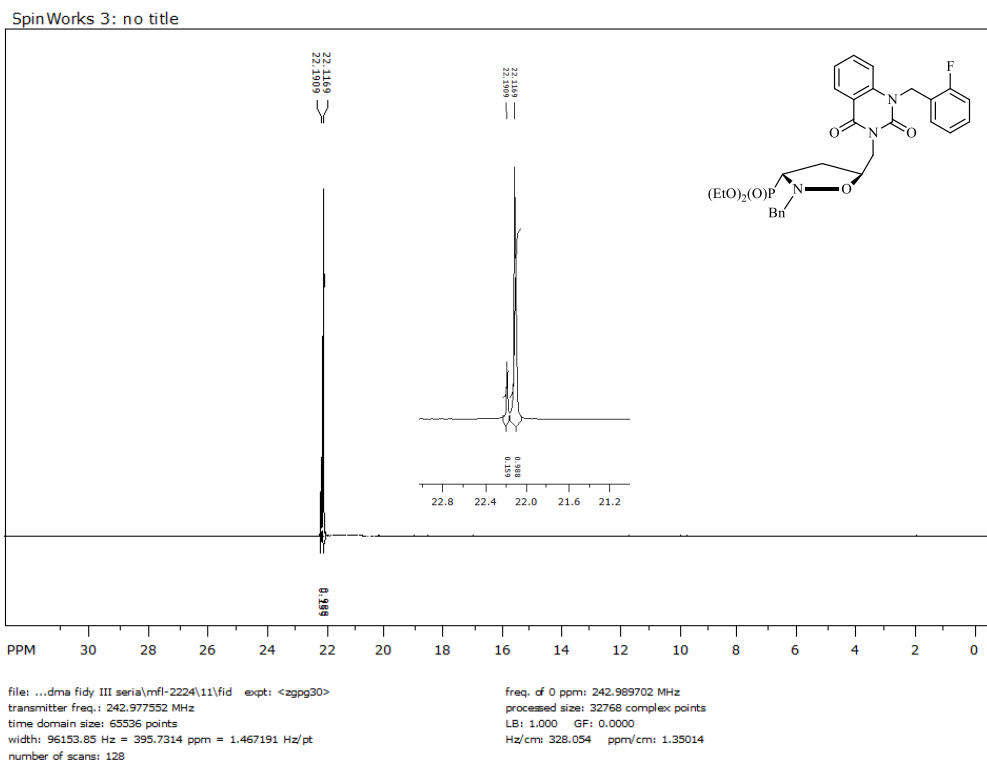


Figure S18: ^{13}C NMR Spectrum for *trans*-**21b** in CDCl_3

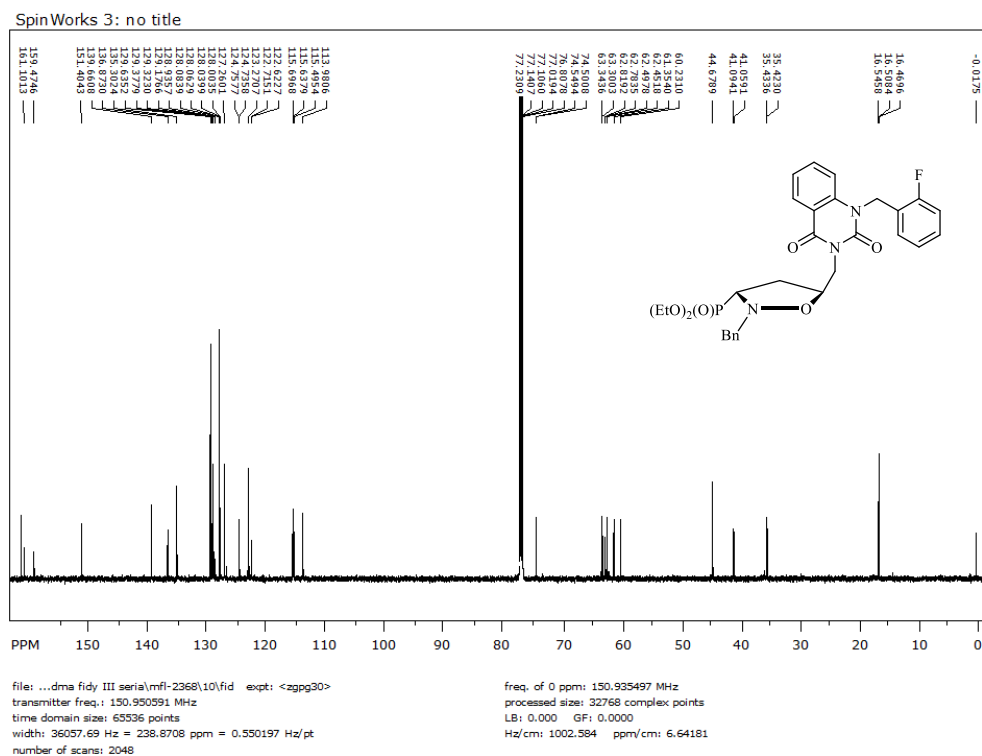


Figure S19: ^1H NMR Spectrum for *trans*-**21c** in CDCl_3

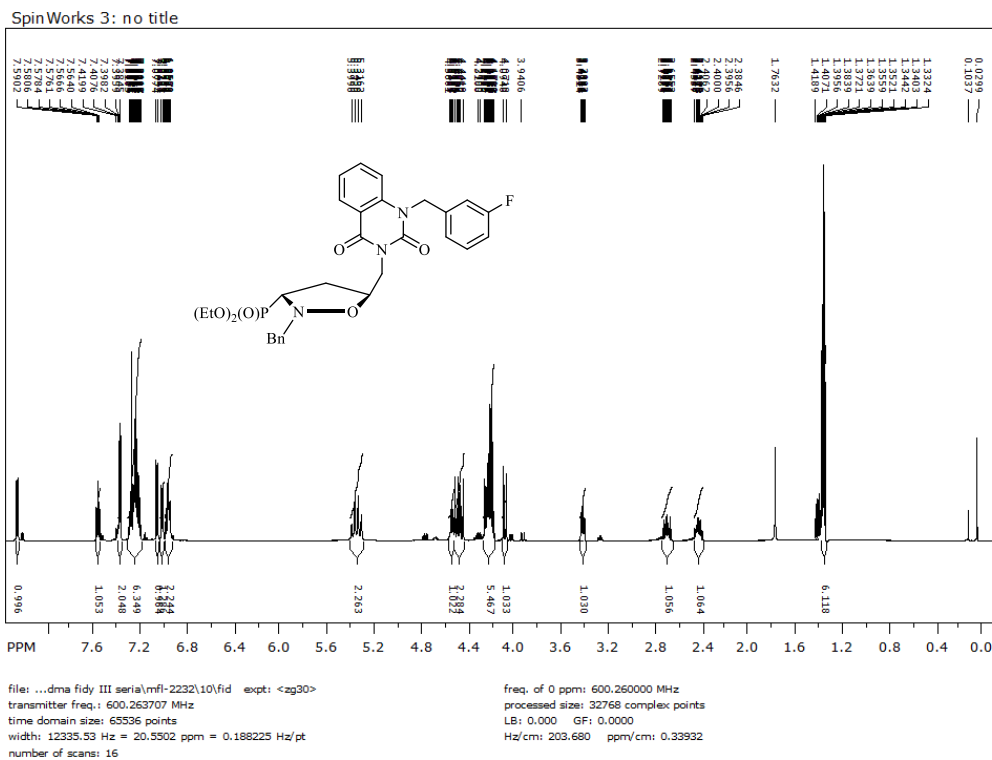


Figure S20: ^{31}P NMR Spectrum for *trans*-**21c** in CDCl_3

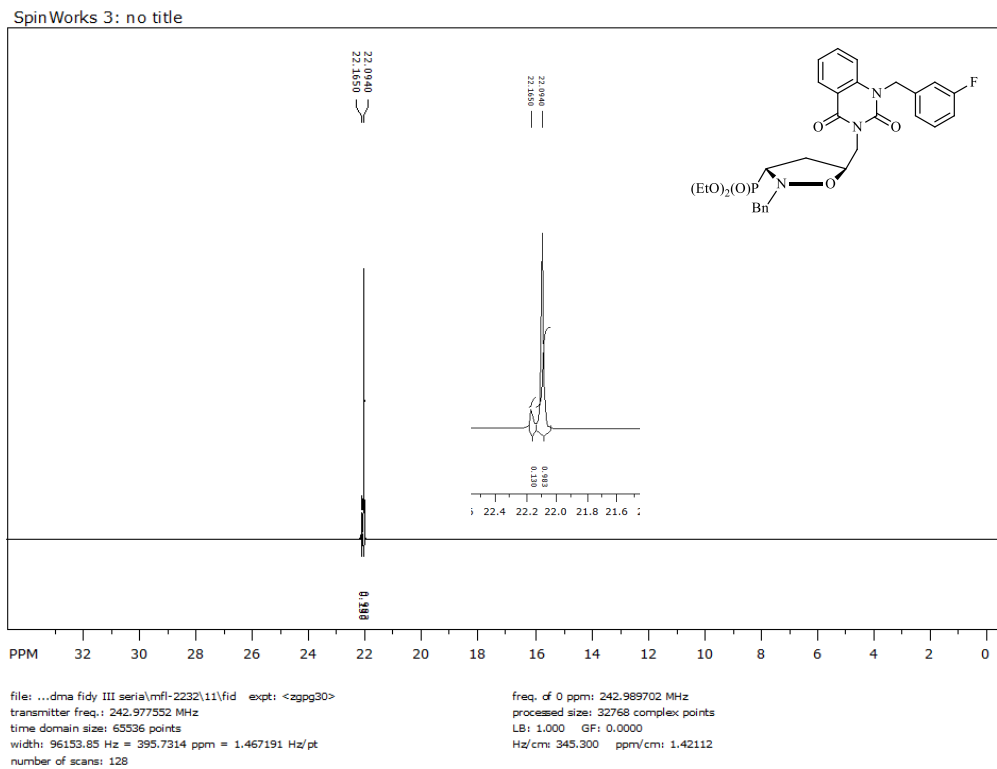


Figure S21: ^{13}C NMR Spectrum for *trans*-**21c** in CDCl_3

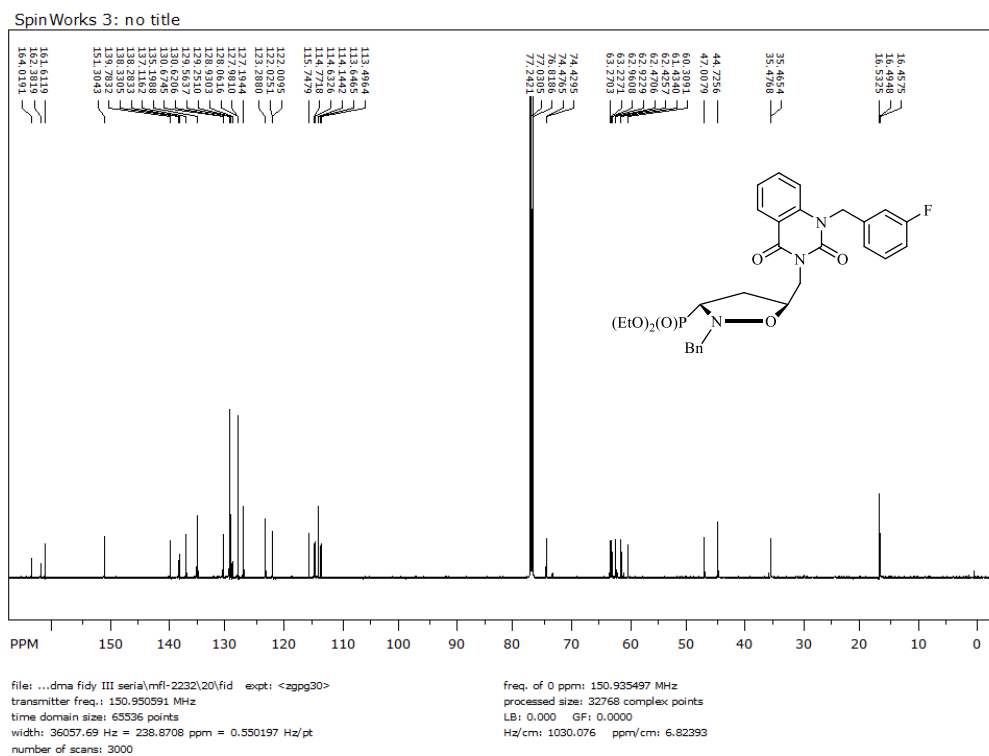


Figure S22: ^1H NMR Spectrum for *trans*-**21d** in CDCl_3

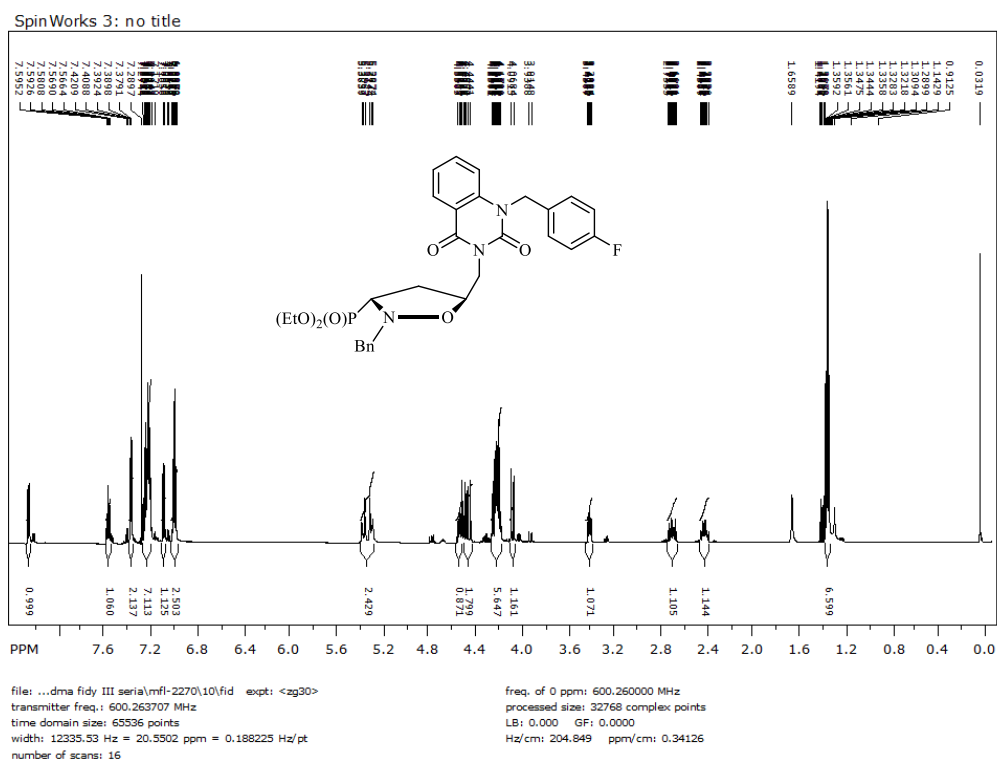


Figure S23: ^{31}P NMR Spectrum for *trans*-**21d** in CDCl_3

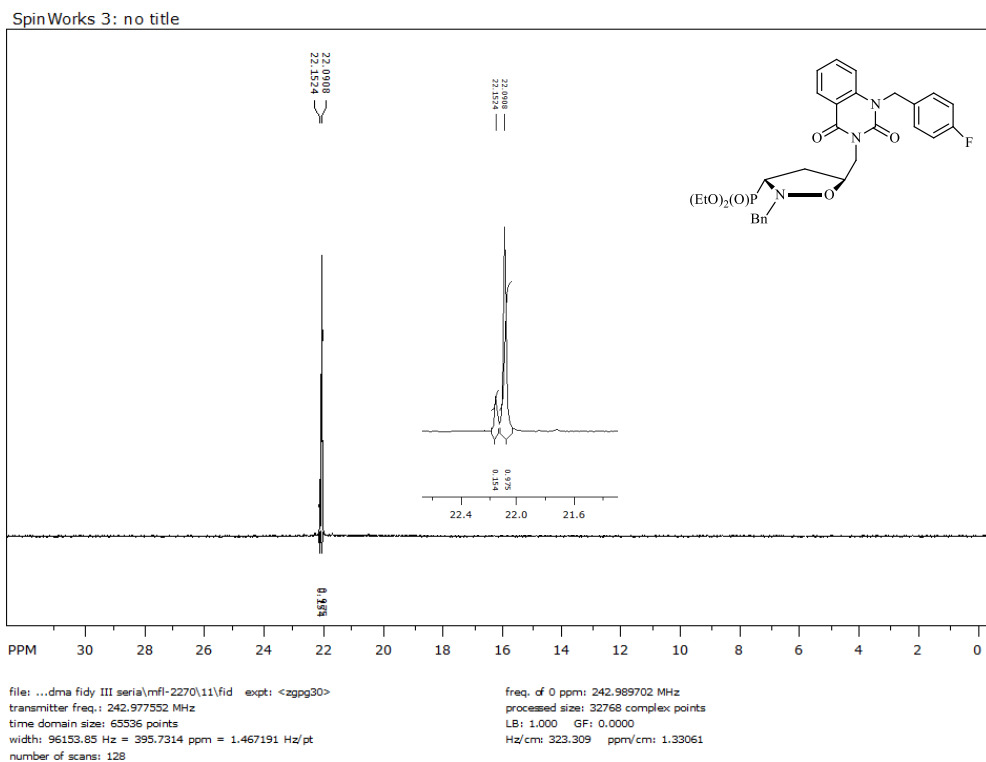


Figure S24: ^{13}C NMR Spectrum for *trans*-**21d** in CDCl_3

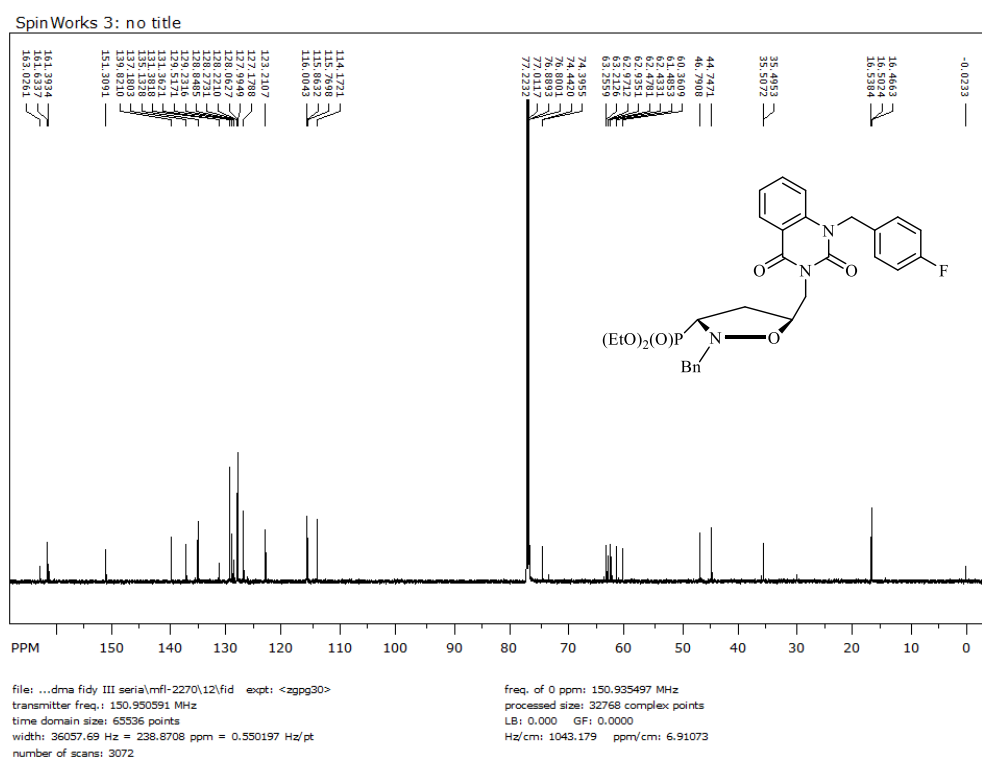


Figure S25: ^1H NMR Spectrum for **24a** in CDCl_3

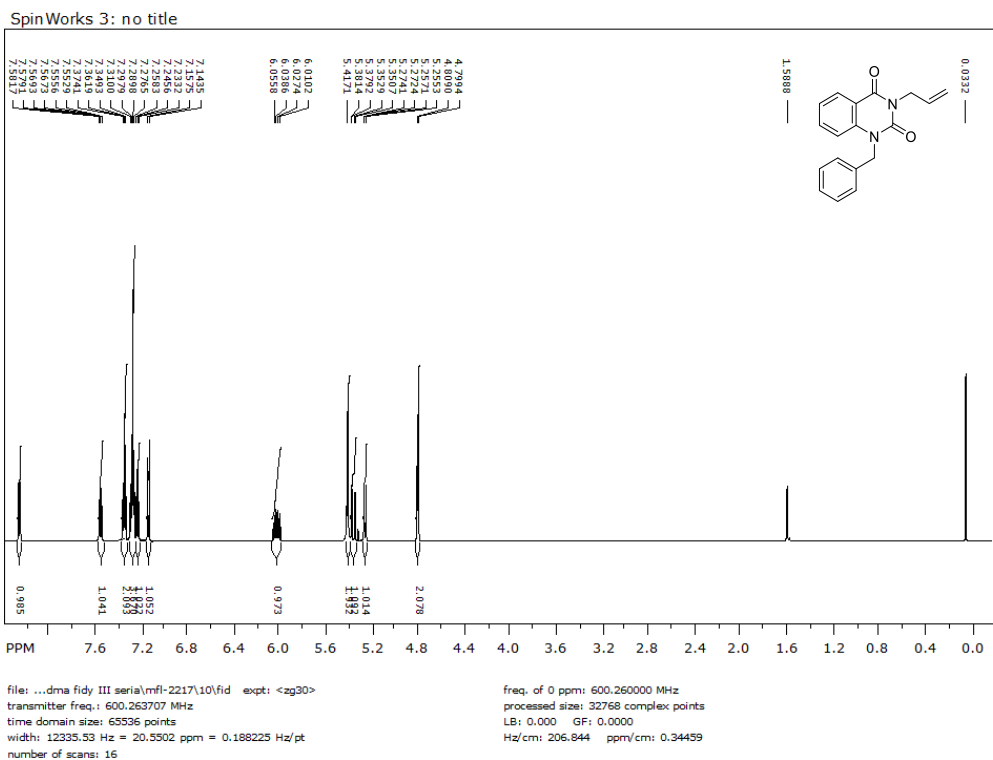


Figure S26: ^{13}C NMR Spectrum for **24a** in CDCl_3

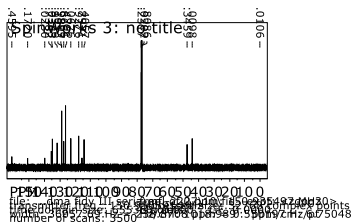


Figure S27: ^1H NMR Spectrum for **24b** in CDCl_3

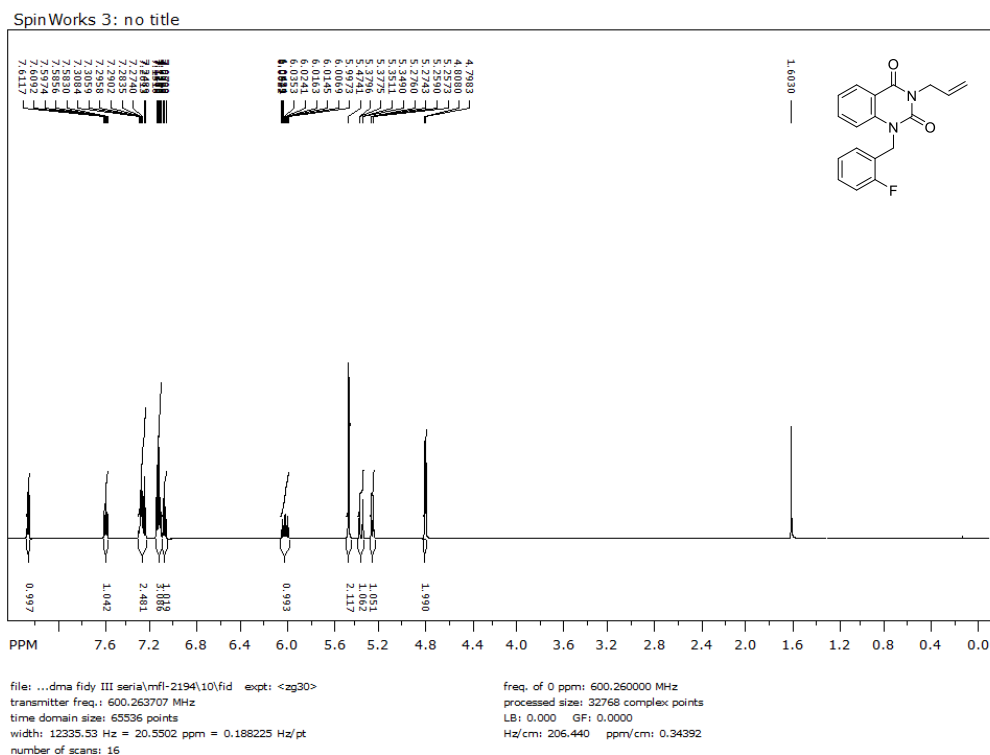


Figure S28: ^{13}C NMR Spectrum for **24b** in CDCl_3

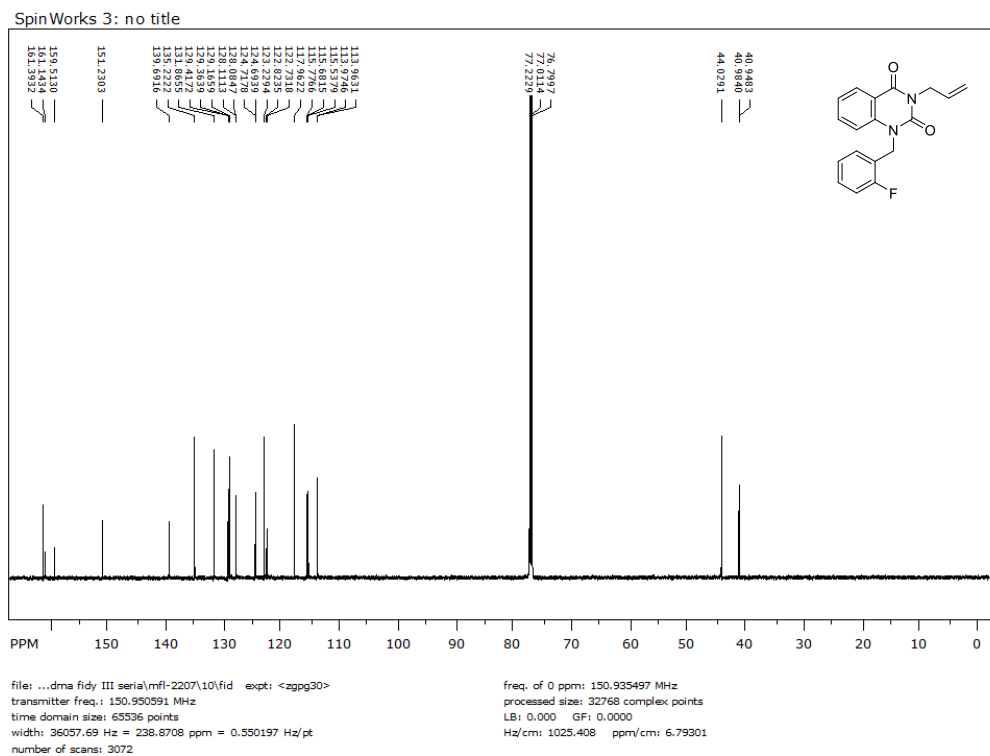


Figure S29: ^1H NMR Spectrum for **24c** in CDCl_3

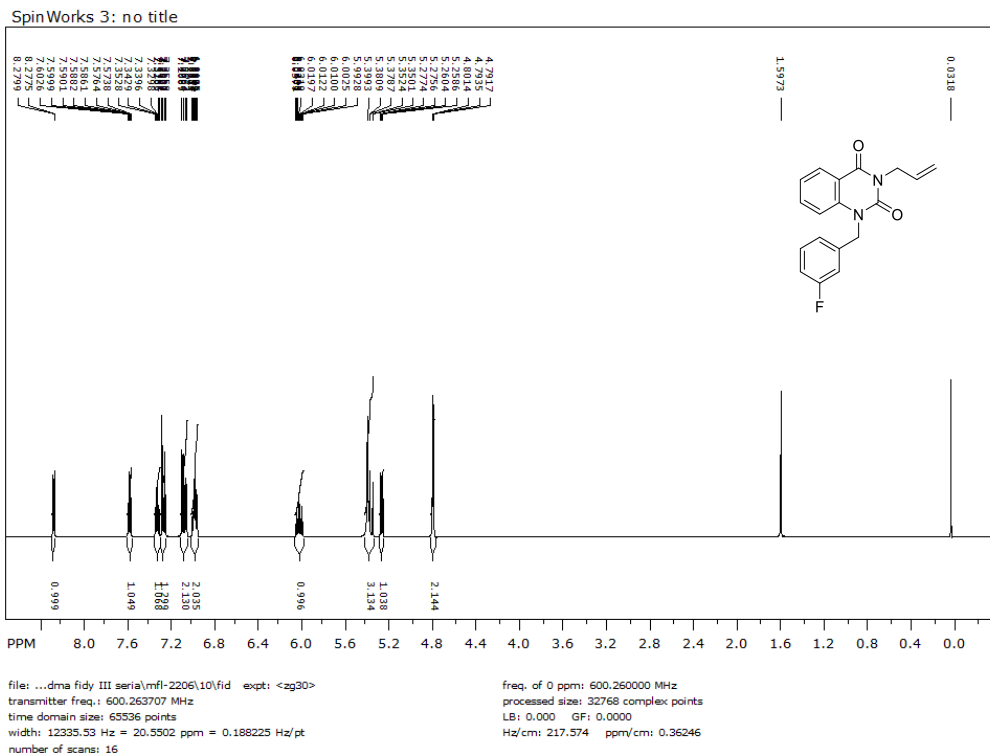


Figure S30: ^{13}C NMR Spectrum for **24c** in CDCl_3

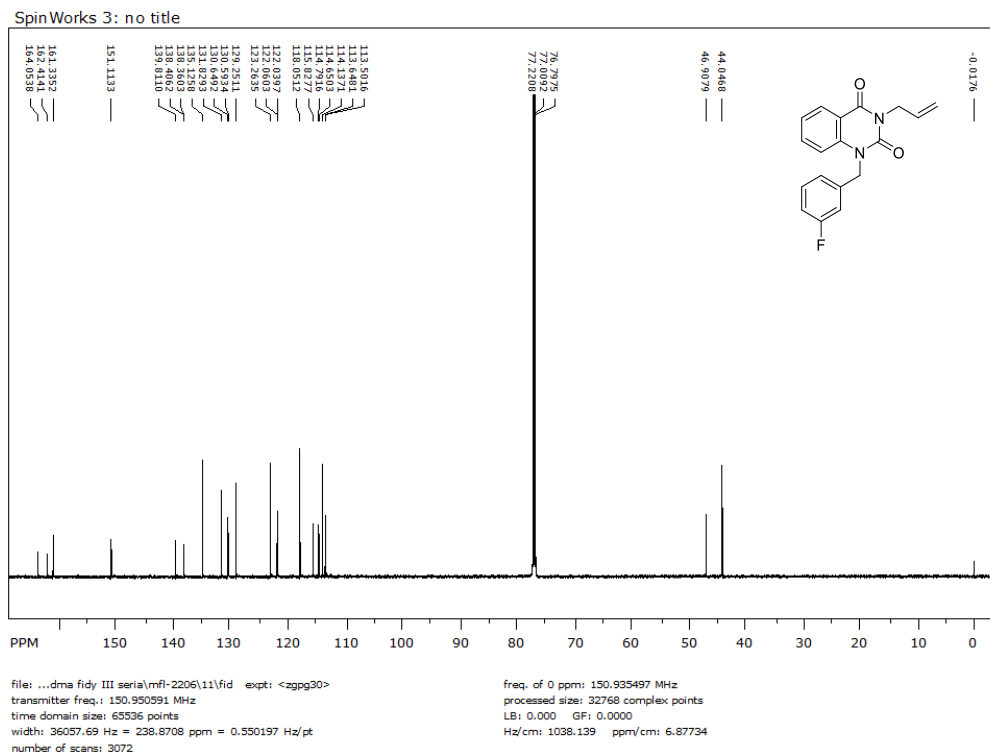


Figure S31: ^1H NMR Spectrum for **24d** in CDCl_3

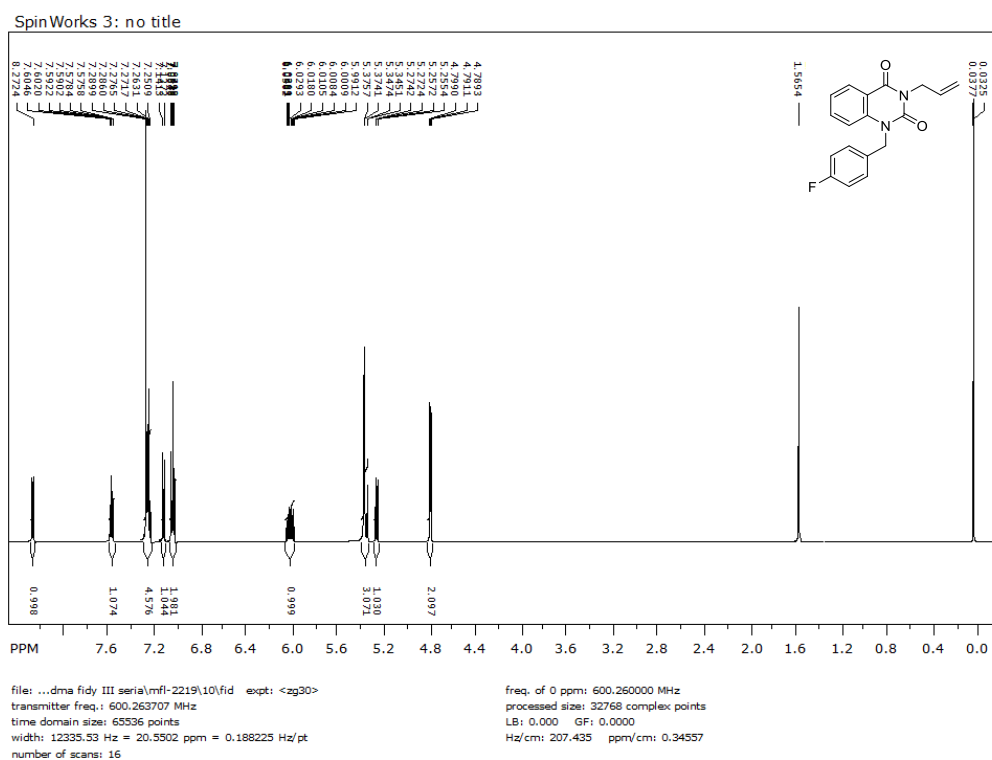


Figure S32: ^{13}C NMR Spectrum for **24d** in CDCl_3

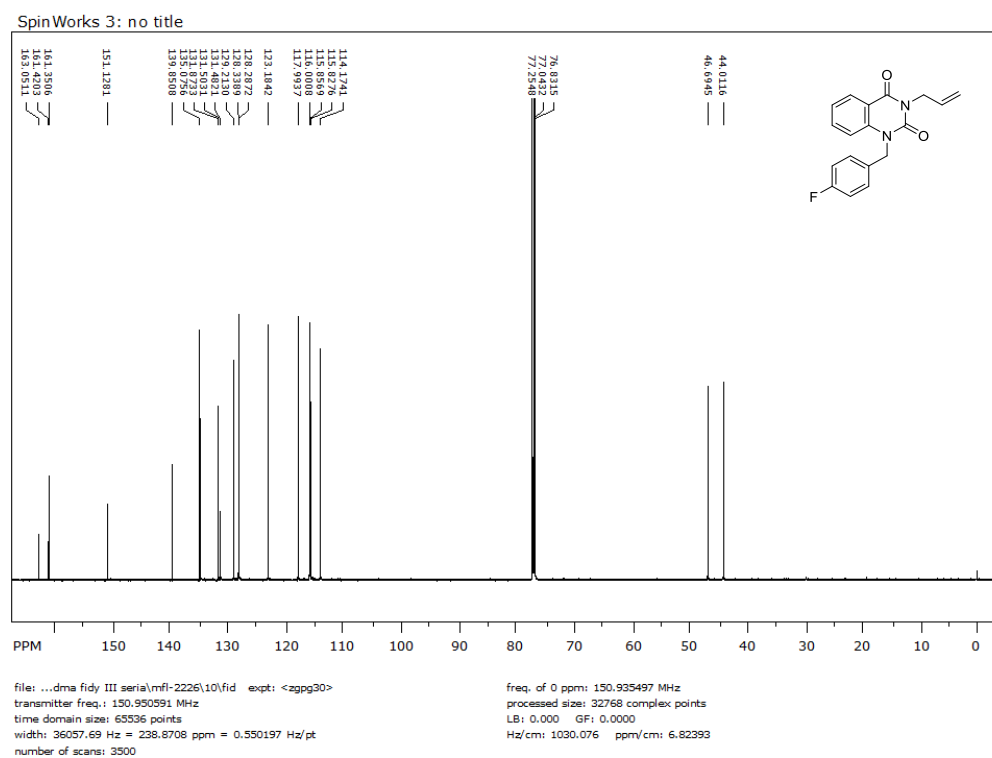


Figure S33: ^1H NMR Spectrum for **26a** in CDCl_3

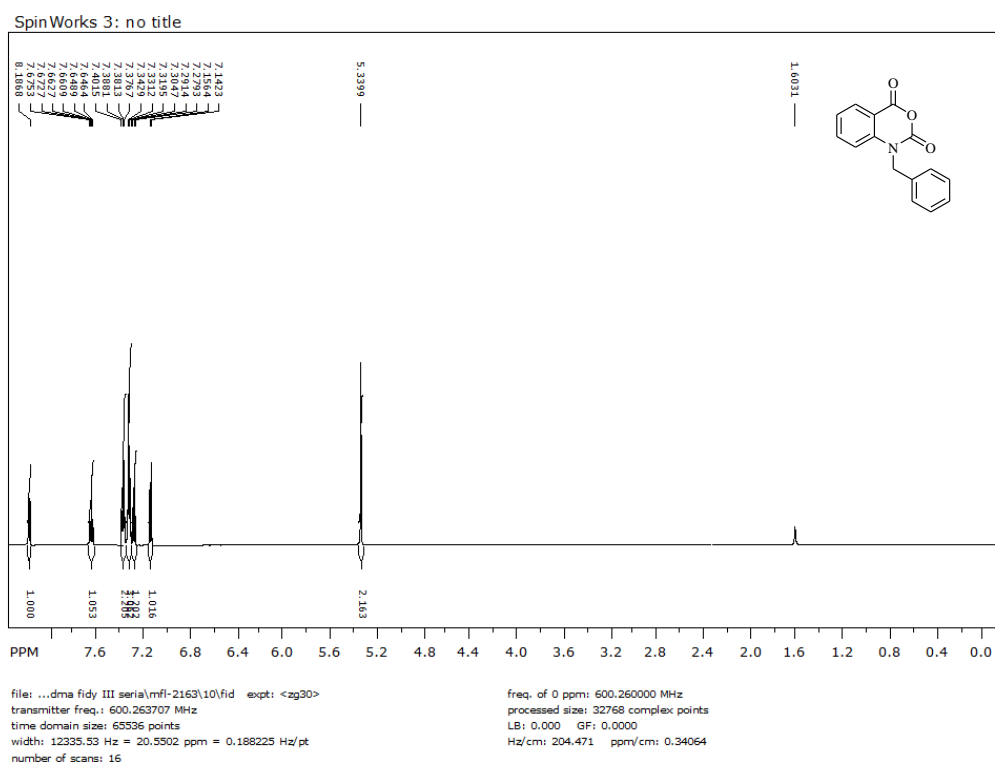


Figure S34: ^{13}C NMR Spectrum for **26a** in CDCl_3

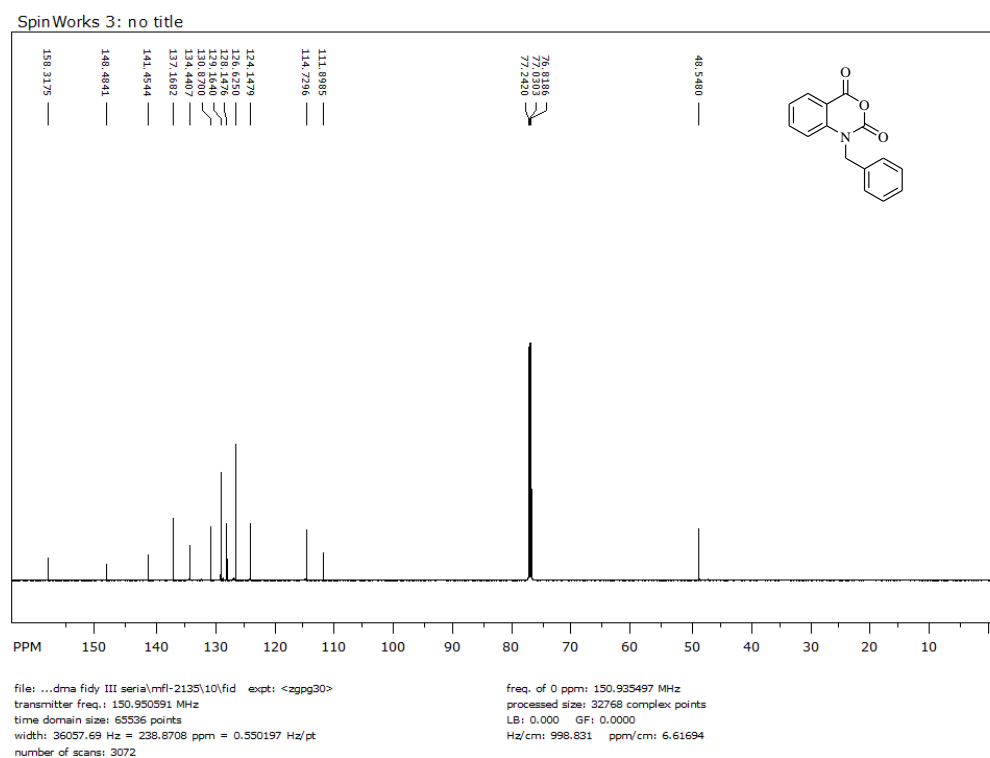


Figure S35: ^1H NMR Spectrum for **26b** in CDCl_3

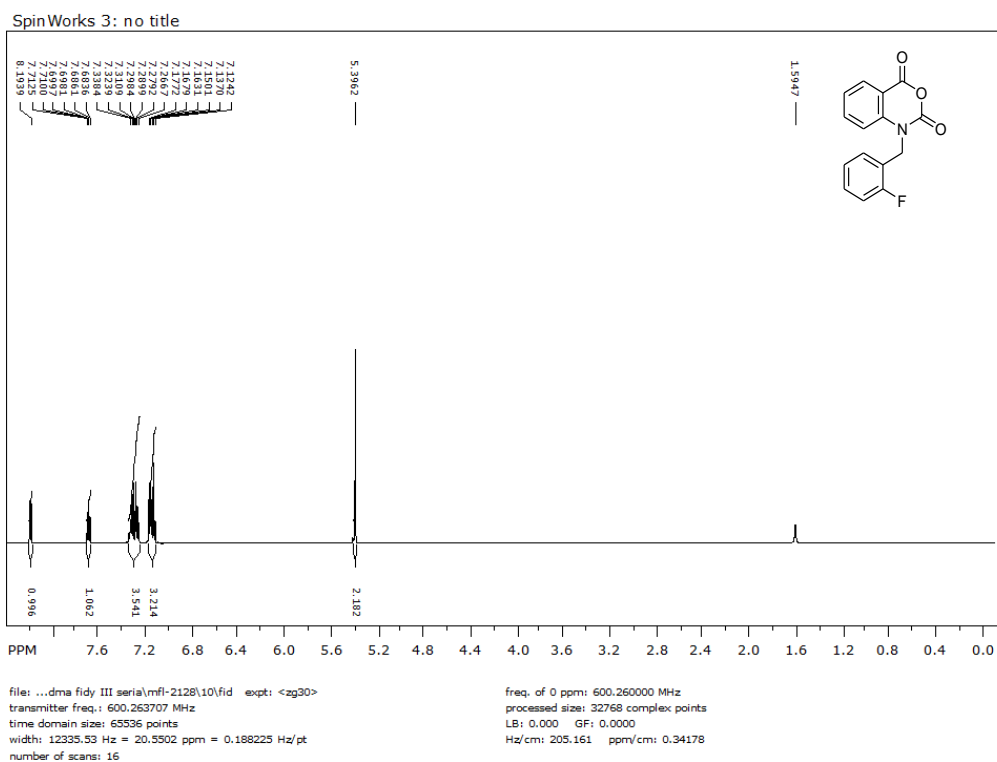


Figure S36: ^{13}C NMR Spectrum for **26b** in CDCl_3

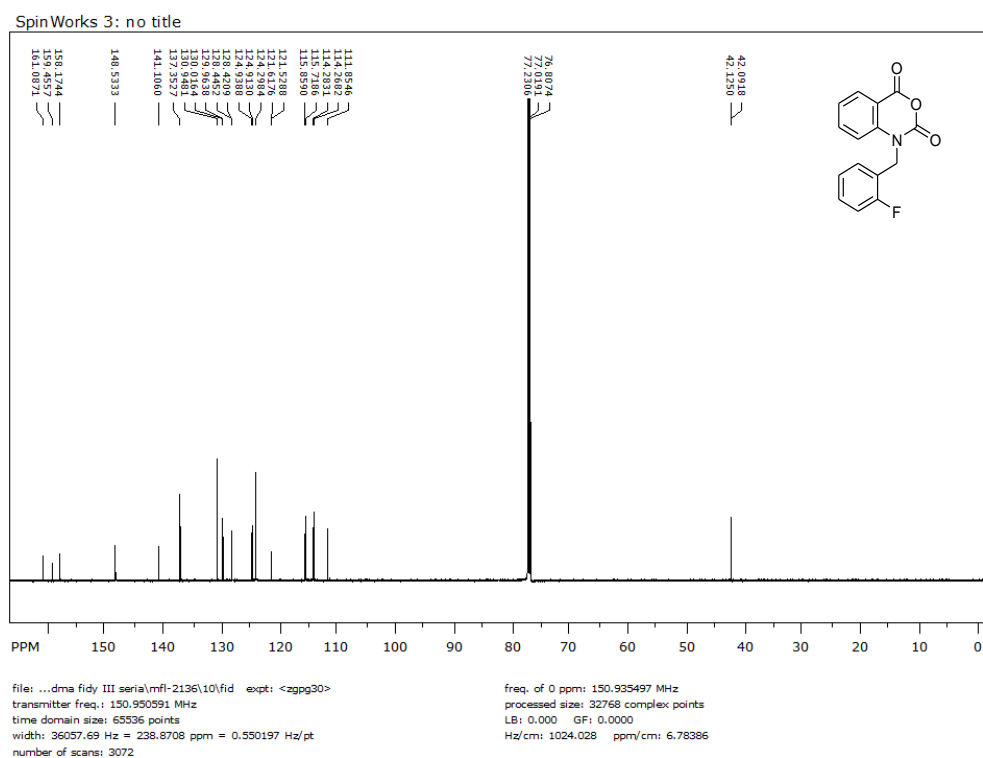


Figure S37: ^1H NMR Spectrum for **26c** in CDCl_3

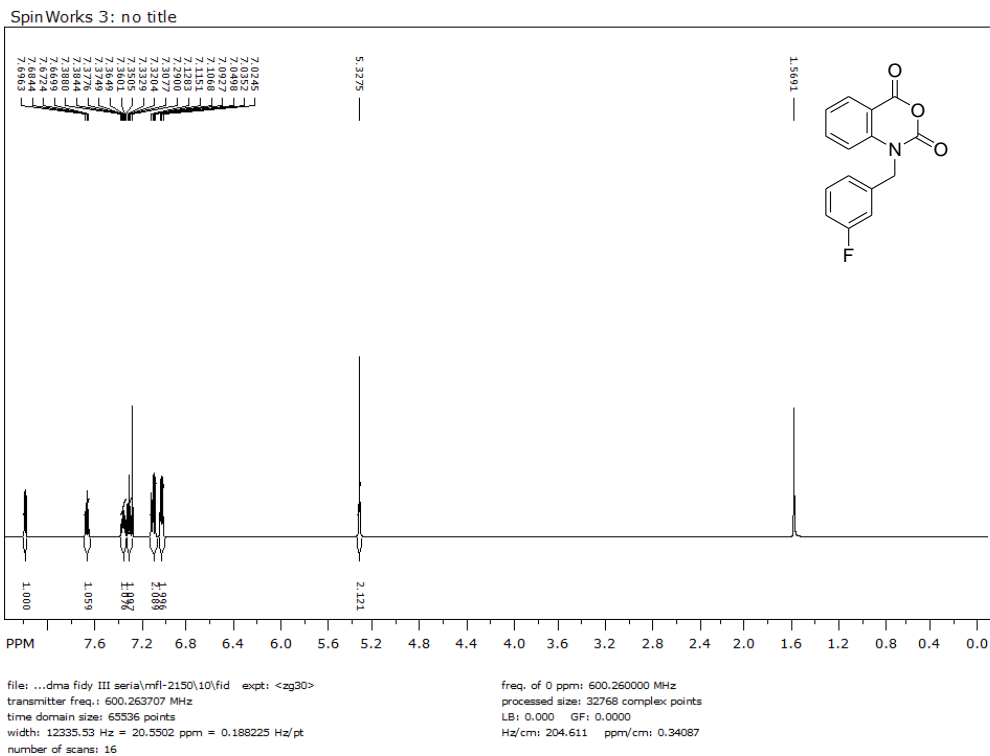


Figure S38: ^{13}C NMR Spectrum for **26c** in CDCl_3

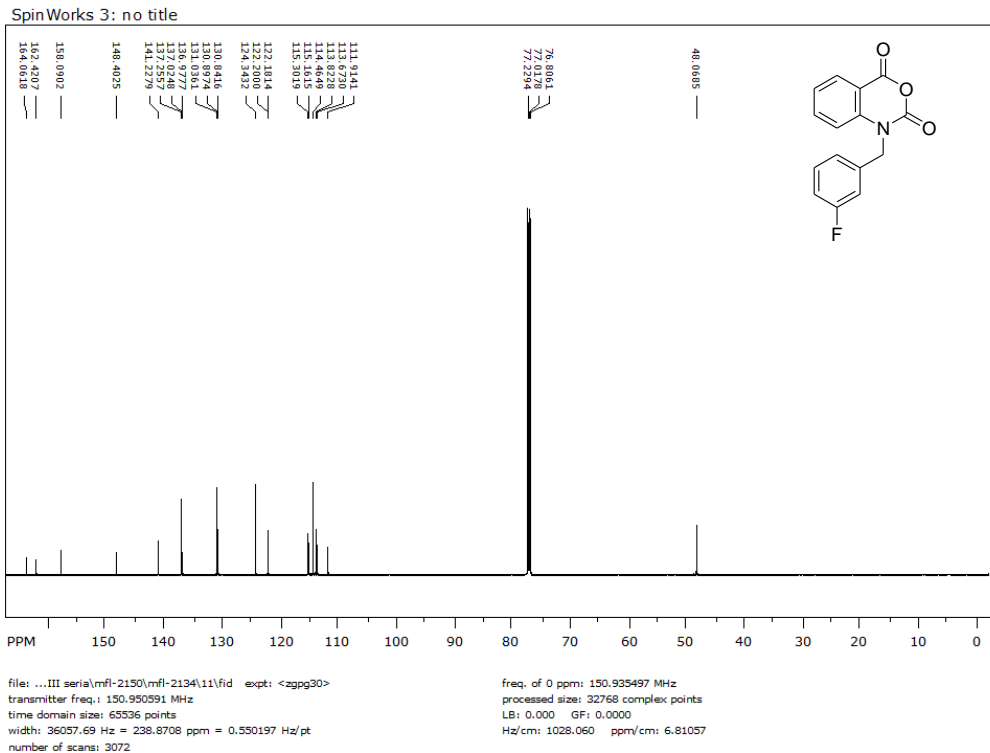


Figure S39: ^1H NMR Spectrum for **26d** in CDCl_3

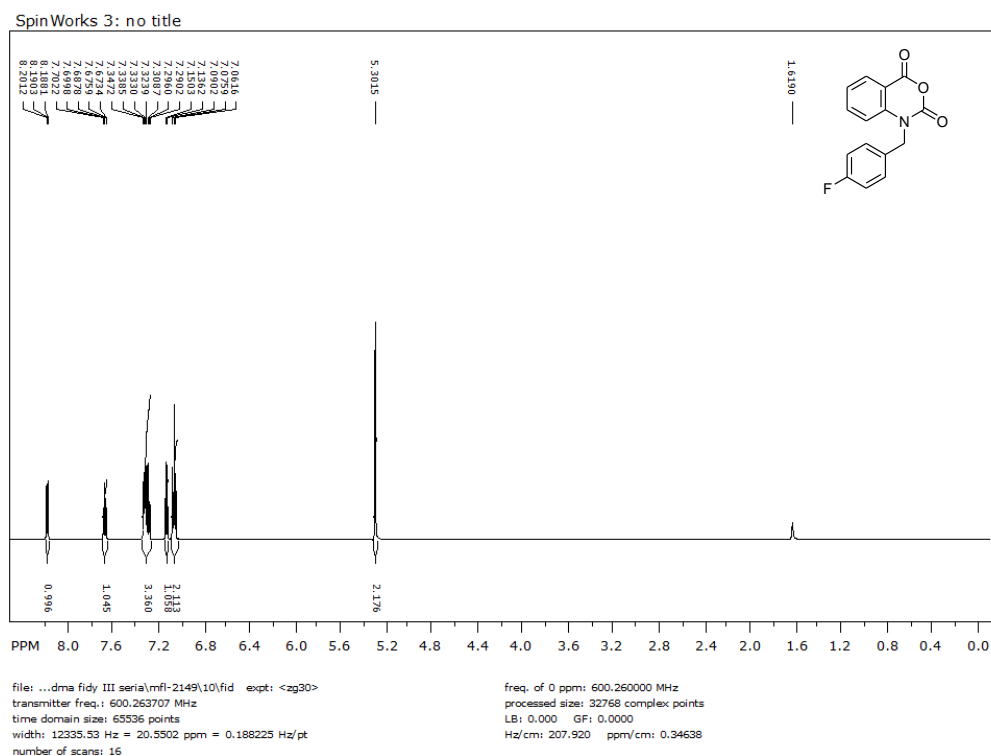


Figure S40: ^{13}C NMR Spectrum for **26d** in CDCl_3

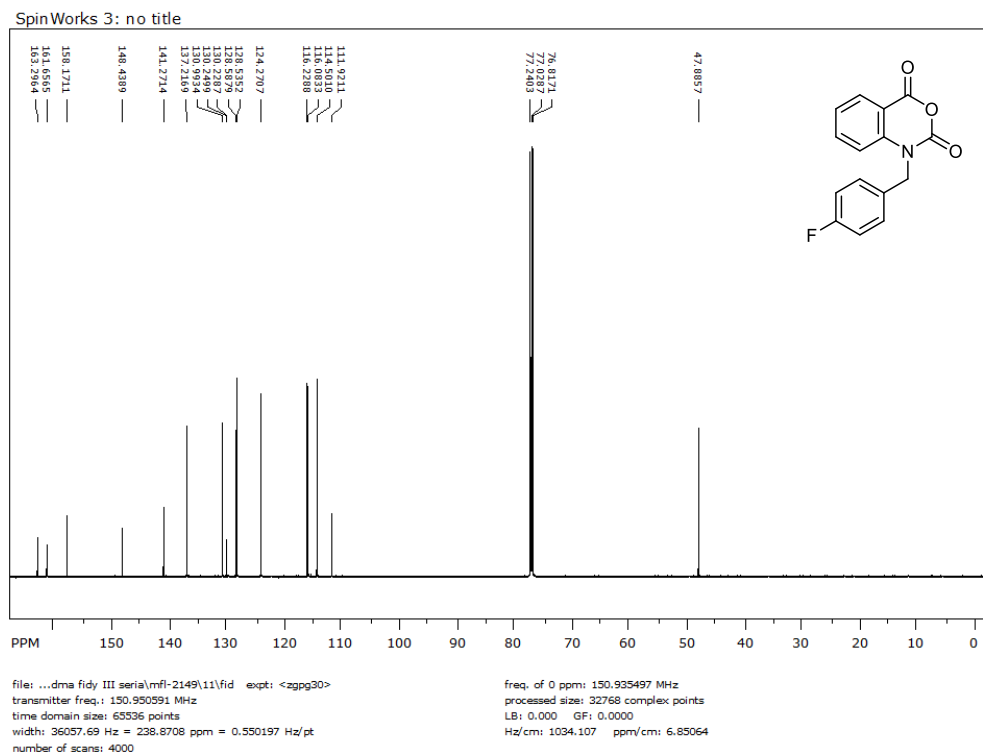


Figure S41: ^1H NMR Spectrum for **27a** in CDCl_3

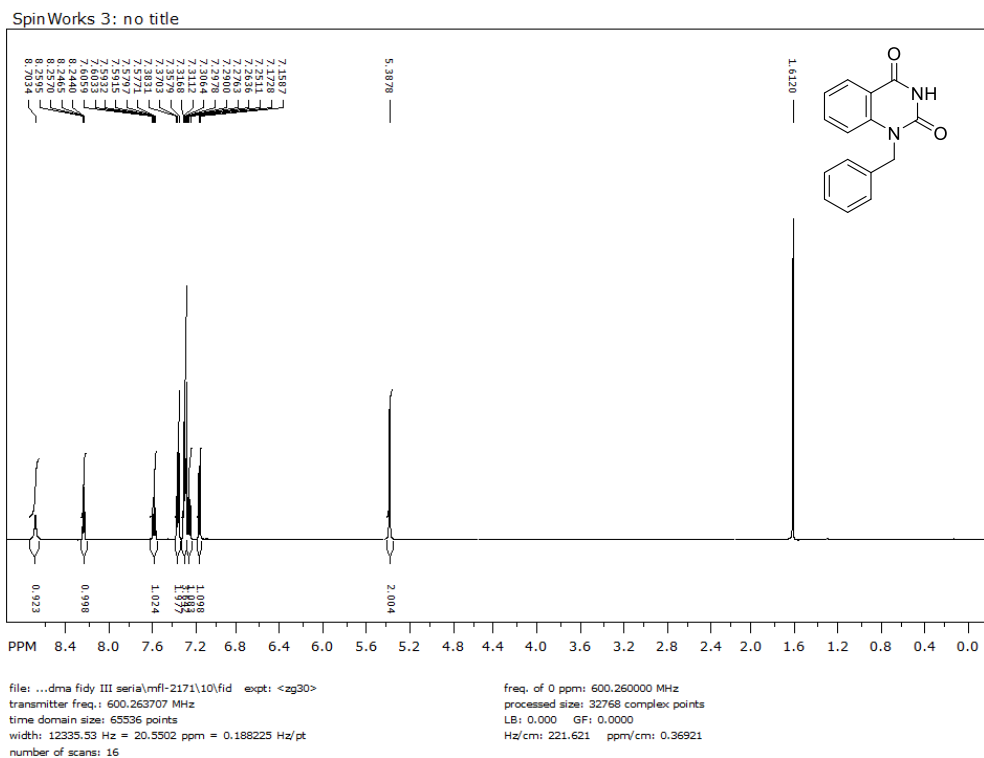


Figure S42: ^{13}C NMR Spectrum for **27a** in CDCl_3

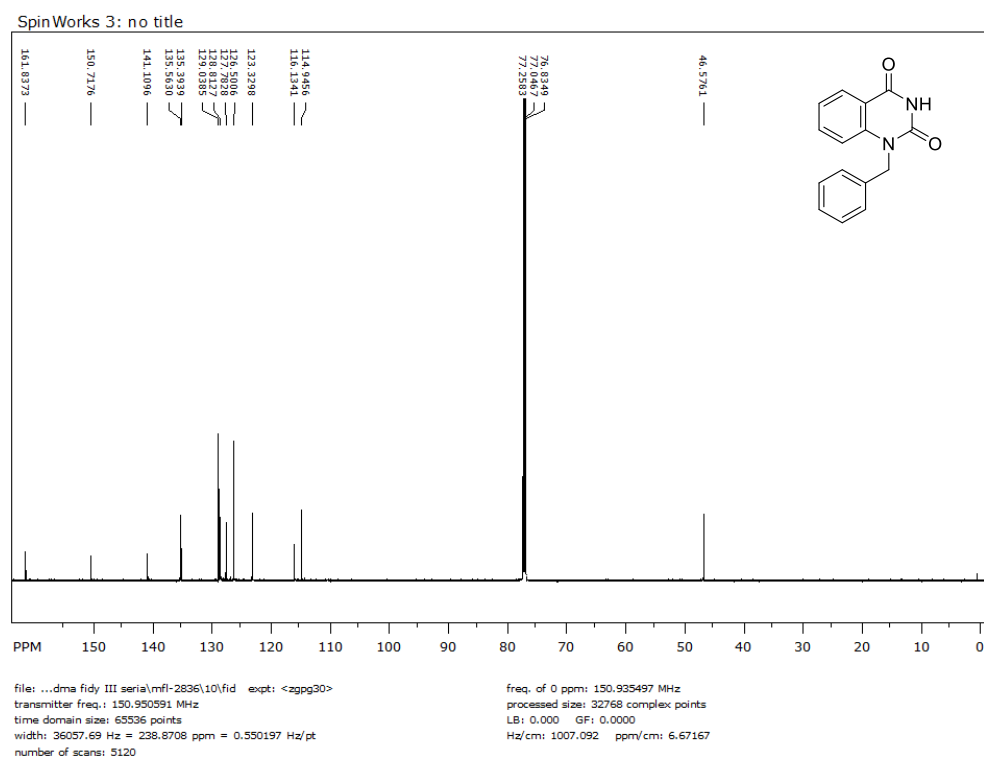


Figure S43: ^1H NMR Spectrum for **27b** in CDCl_3

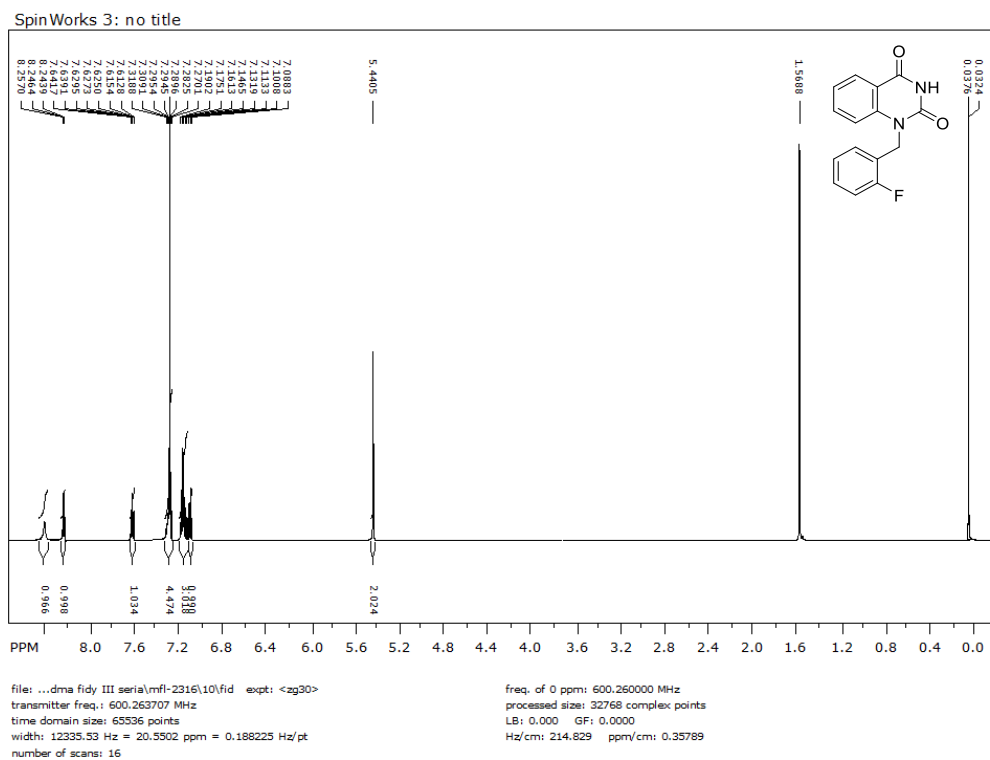


Figure S44: ^{13}C NMR Spectrum for **27b** in CDCl_3

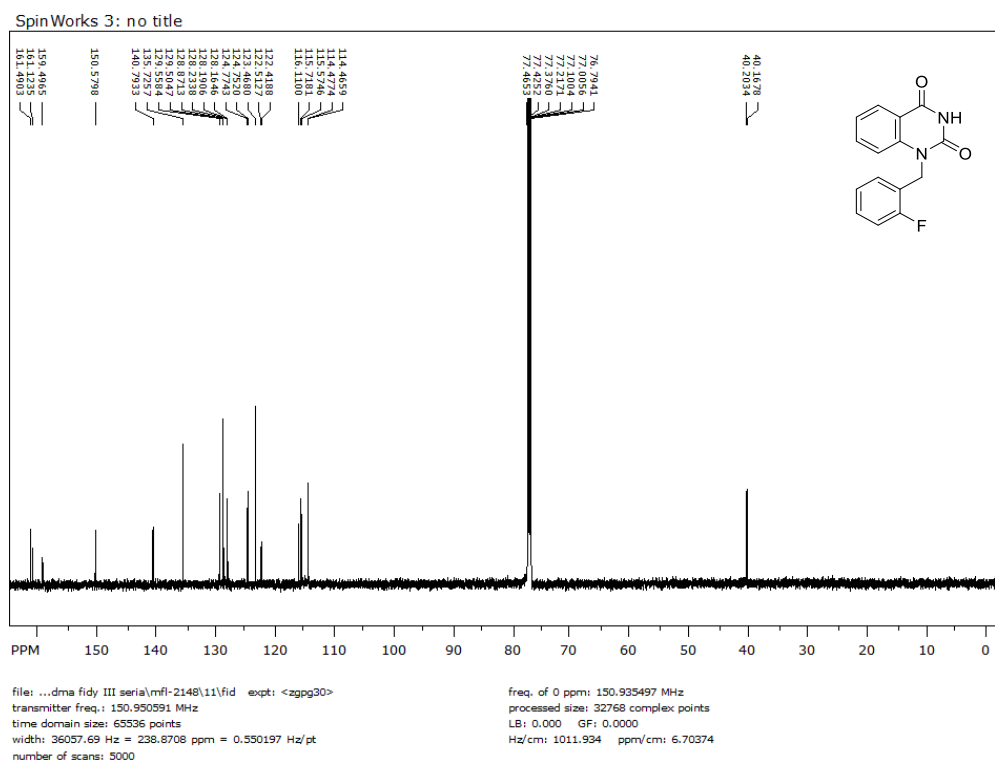


Figure S45: ^1H NMR Spectrum for **27c** in CDCl_3

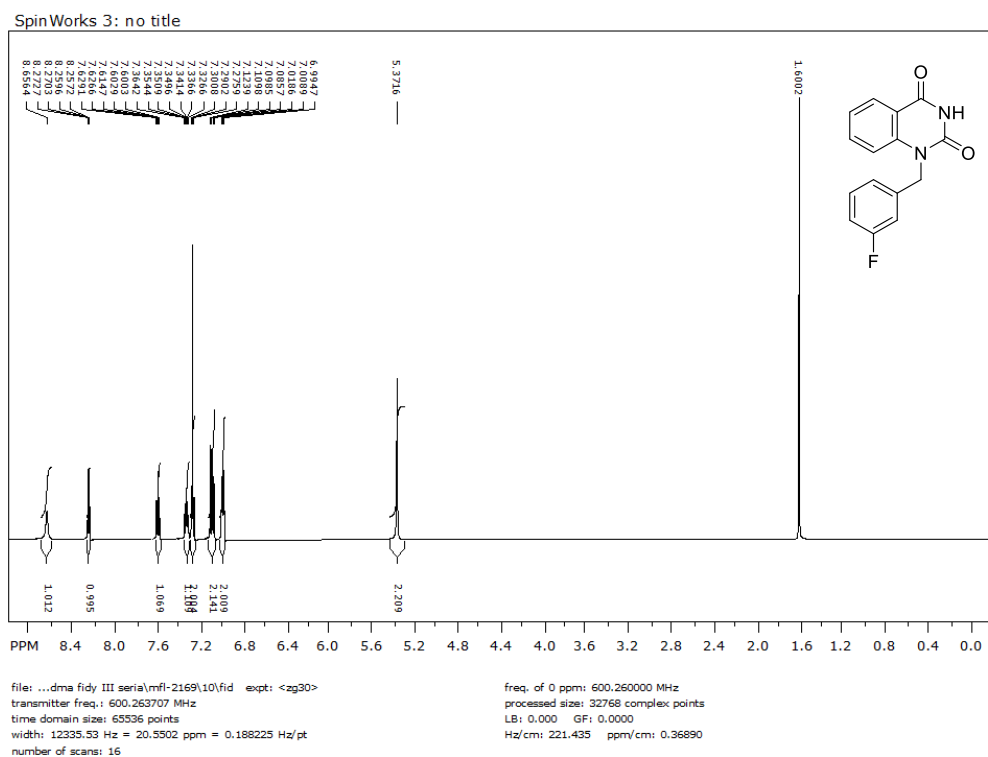


Figure S46: ^{13}C NMR Spectrum for **27c** in CDCl_3

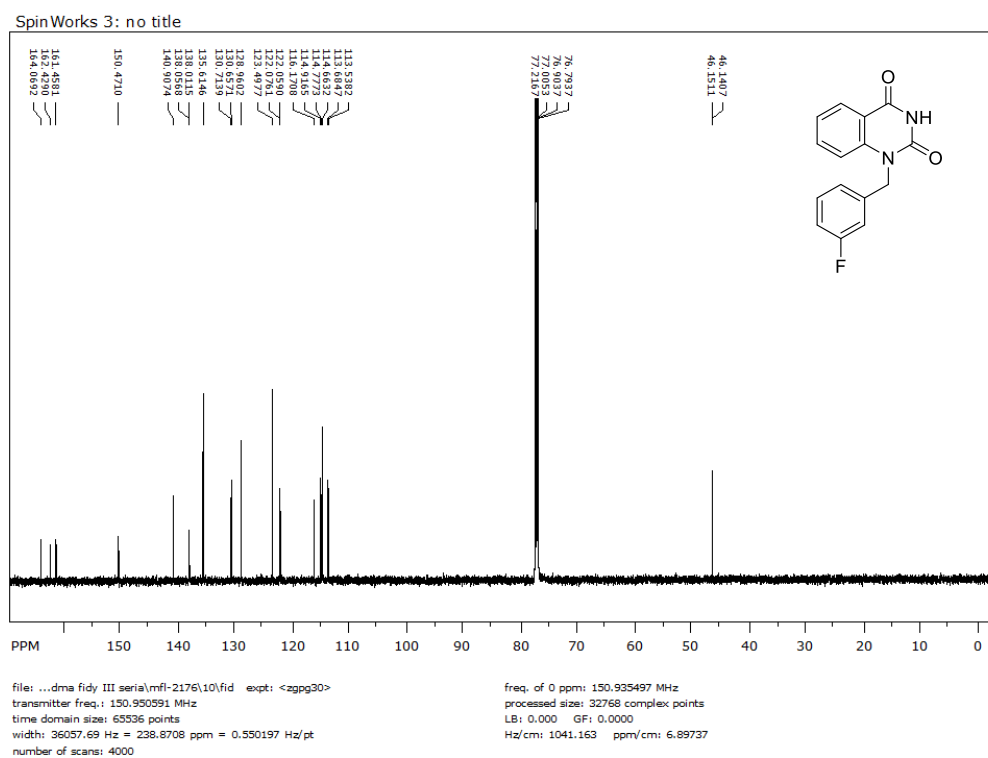


Figure S47: ^1H NMR Spectrum for **27d** in CDCl_3

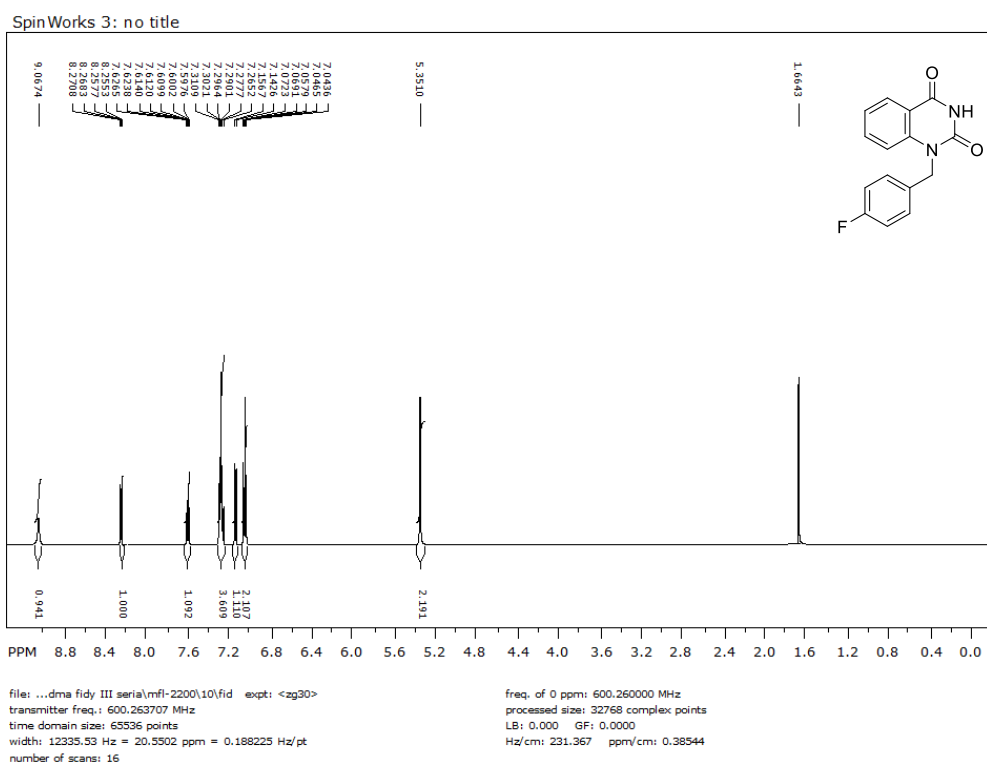


Figure S48. ^{13}C NMR Spectrum for **27d** in CDCl_3

