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Effect of pH on the reaction outcome between tetraacetyl hexaazaisowurtzitane and aldehydes

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3,5,9,11-Tetraacetyl-14-oxa-1,3,5,7,9,11-hexaazapentacyclo[5.5.3.$0^{2,6}$.$0^{4,10}$.$0^{8,12}$]pentadecane (2). To a suspension of TAIW **1** (3.36 g, 0.01 mol) in acetonitrile (15 ml), formaldehyde solution (37% aq., 1.4 ml, 0.02 mol) was added at room temperature. The pH value was controlled and the consumption of the starting compound was monitored. The resulting solution was filtered, evaporated, the solid was dried in air. Mp 385°C. IR (ν/cm^{-1}): 3027, 2981, 2900, 1687, 1658, 1389, 1353, 1269, 1191, 1125, 1043, 1000, 956, 901, 843, 792, 728, 683, 607. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ: 2.00-2.04(m, 12H, CH_3), 4.56-4.72 (m, 4H, CH_2), 5.42-5.58 (m, 4H, CH), 6.19-6.37(m, 2H, CH). ^{13}C NMR (100.61 MHz, DMSO-d_6) δ: 21.86, 22.40, 57.27, 57.87, 65.22, 66.19, 70.53, 71.09, 162.44, 166.64, 167.35, 167.23. $C_{16}H_{22}N_6O_5$: Calc., %: 50.79 (C); 5.86 (H); 22.21 (N); 21.14 (O). Found, %: 50.73 (C); 5.81 (H); 22.34 (N); 21.12 (O)

4-(1-Hydroxyethyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane (3a). To a suspension of TAIW **1** (3.36 g, 0.01 mol) in acetonitrile (40 ml), acetaldehyde (2.30 ml, 0.02 mol) was added at room temperature, and the reaction was carried out under pH control until decomposition emerged (color changes of the solution). The resulting precipitate was filtered off and recrystallized from a 1:4 water-methanol mixture, with this, hot filtration provided removal of unreacted TAIW **1**. The recrystallized precipitate was air dried, mp 342 °C. IR (ν/cm^{-1}): 3270, 3191, 3031, 2974, 1675, 1658, 1389, 1353, 1269, 1191, 1125, 1043, 1000, 956, 901, 843, 792, 728, 683, 604, 593. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ: 1.23 (t, 3H, CH_3), 1.80 (s, H, CH), 1.91-2.07 (m, 12H, CH_3), 4.13-4.32(m, H, NH), 5.24-5.50 (m, 4H, CH), 6.12-6.34 (m, 2H, CH), 7.94 (s, H, OH). ^{13}C NMR (100.61 MHz, DMSO-d_6) δ: 22.54, 22.96, 24.31, 57.27, 57.87, 63.51, 66.03, 66.78, 70.51, 71.18, 160.25, 161.37, 163.41. $C_{16}H_{24}N_6O_5$: Calc., %: 50.52 (C); 6.36 (H); 22.09 (N); 21.03 (O). Found, %: 50.43 (C); 6.40 (H); 22.10 (N); 21.07 (O).

4-(1-Hydroxypropyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane (3b). To a suspension of TAIW **1** (3.36 g, 0.01 mol) in acetonitrile (40 ml), propanal (1.70 ml, 0.022 mol) was added at room temperature, and the reaction was carried out under pH control until decomposition emerged (color changes of the solution). The resulting precipitate was filtered off and recrystallized from a 1:4 water-methanol mixture, with this, hot filtration provided removal of unreacted TAIW **1**. The recrystallized precipitate was air dried, mp 345°C. IR (ν/cm^{-1}): 3380, 3201, 3038, 2985, 1681,

1658, 1389, 1353, 1237, 1192, 1124, 1041, 997, 956, 904, 840, 781, 723, 686, 607, 593. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ: 1.78-2.08 (m, 16H, CH, CH_3), 2.73 (s, H, CH_2), 2.89 (s, H, CH_2), 4.13-4.31 (m, H, NH), 5.32-5.56 (m, 4H, CH), 6.12-6.45 (m, 2H, CH), 8.23 (s, H, OH). ^{13}C NMR (100.61 MHz, DMSO-d_6) δ: 12.58, 22.25, 22.54, 25.26, 57.28, 57.94, 66.18, 66.65, 70.19, 71.21, 71.40, 164.35, 166.14, 167.43. $C_{17}H_{26}N_6O_5$: Calc., %: 51.77 (C); 6.64 (H); 21.31 (N); 20.28 (O). Found, %: 51.70 (C); 6.63 (H); 21.30 (N); 20.37 (O).

4-(1-Hydroxybutyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane (3c). To a suspension of TAIW **1** (3.36 g, 0.01 mol) in acetonitrile (40 ml), butanal (2.2 ml, 0.022 mol) was added at room temperature, and the reaction was carried out under pH control until decomposition emerged (color changes of the solution). The resulting precipitate was filtered off and recrystallized from a 1:4 water-methanol mixture, with this, hot filtration provided removal of unreacted TAIW **1**. The recrystallized precipitate was air dried, mp 340 °C. IR (ν/cm^{-1}): 3345, 3187, 3012, 2995, 1676, 1558, 1377, 1351, 1232, 1194, 1119, 1043, 998, 955, 902, 841, 785, 724, 687, 605, 591. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ: 1.28 (s, 2H, CH_2), 1.47-1.51 (t, 3H, CH_3), 1.79-2.01 (m, 12H, CH_3), 2.09-2.28 (m, 2H, CH_2), 4.13-4.31 (m, H, NH), 5.00 (s, H, CH), 5.32-5.57 (m, 4H, CH), 6.12-6.45 (m, 2H, CH), 8.11 (s, H, OH). ^{13}C NMR (100.61 MHz, DMSO-d_6) δ: 14.58, 17.51, 21.27, 22.51, 32.43, 57.28, 57.94, 66.18, 66.65, 69.22, 71.02, 73.28, 164.21, 165.73, 167.15. $C_{17}H_{26}N_6O_5$: Calc., %: 52.93 (C); 6.91 (H); 20.58 (N); 19.59 (O). Found, %: 52.90 (C); 6.88 (H); 20.55 (N); 19.67 (O).

4-(*N*-Benzylaminomethyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane (4a). A suspension of TAIW **1** (13.2 g, 0.04 mol) in water (54 ml) was prepared, and the required pH value was achieved by adding formic acid or sodium carbonate. Benzylamine (9 ml, 0.08 mol) and formaldehyde solution (37% aq., 6 ml, 0.08 mol) were added simultaneously from two dropping funnels at room temperature within 1 h. The reaction was then carried out until decomposition emerged (color change of the solution). The resulting precipitate was filtered off and washed with chloroform to remove 1,3,5-tribenzyl-1,3,5-triazacyclohexane. The product was air dried, mp 330 °C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ: 1.97-2.03 (m, 12H, CH_3), 4.68 (s, 4H, CH_2), 4.80-4.81 (br.s, H, NH), 5.49-5.58 (m, 4H, CH), 6.19-6.39 (m, 2H, CH), 7.93 (s, $5H_{arom}$). ^{13}C NMR (100.61 MHz, DMSO-d_6) δ: 21.34, 21.87, 22.82, 32.43, 42.52, 64.91, 66.34, 67.49, 70.07, 71.22, 72.37, 128.81, 129.06, 129.50, 134.60, 164.84, 165.33, 165.92. $C_{22}H_{29}N_7O_4$: Calc., %: 58.01 (C); 6.42 (H); 21.52 (N); 14.05 (O). Found, %: 57.87 (C); 6.47 (H); 21.61 (N); 14.07 (O).

4-Morpholinomethyl-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzite (4b). To a suspension of TAIW **1** (3.36 g, 0.01 mol) in acetonitrile (30 ml) morpholine (1.8 ml, 0.02 mol) was added followed by formaldehyde solution (37% aq., 1.5 ml, 0.02 mol). The reaction was then carried out at pH control until decomposition emerged (color change of the solution). The resulting precipitate was filtered off, treated with a 1:4 water-methanol mixture, and unreacted TAIW was

removed. The filtrate was placed in a refrigerator for 2 days. The precipitated crystals were dried in air, mp 290°C. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ: 2.02-2.10(m,12H,CH_3), 2.44 (s, 4H, CH_2), 2.83 (s, H, CH_2), 3.15 (s, H, CH_2), 3.34-3.40 (m, 4H, CH_2), 4.21-4.42 (br.s, H, NH), 5.36-5.56 (m, 4H, CH), 6.12-6.49 (m, 2H, CH). ^{13}C NMR (100.61 MHz, DMSO-d_6) δ: 21.79, 22.40, 22.72, 23.17, 42.97, 57.28, 57.94, 58.80, 63.58, 65.17, 66.11, 66.84, 70.32, 71.02, 73.28, 165.00, 165.27, 166.30. $C_{19}H_{29}N_7O_5$: Calc., %: 52.40 (C); 6.71 (H); 22.51 (N); 18.37 (O). Found, %: 52.46 (C); 6.71 (H); 22.54 (N); 18.29 (O).

The structures of the resultant compounds were validated by NMR and IR spectroscopies using instruments provided by the Biysk Regional Center for Shared Use of Scientific Equipment "Center for Synthesis and Research into High-Energy Compounds and Specialty Materials" of the SB RAS.

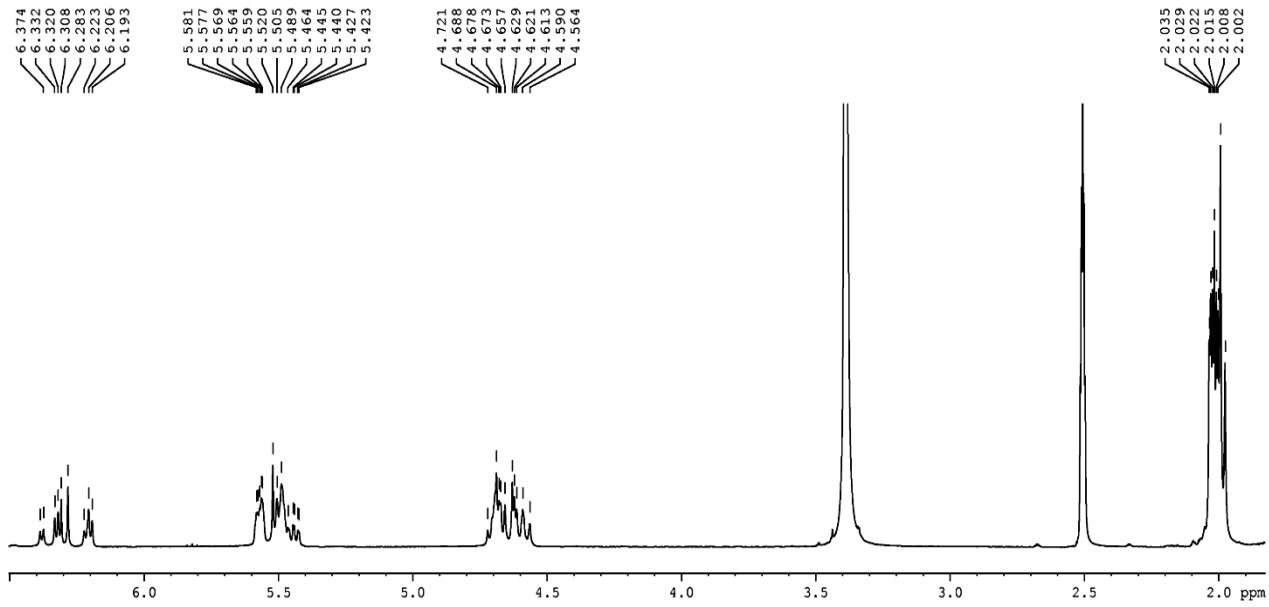

Figure S1 ^{1}H NMR 3,5,9,11-tetraacetyl-14-oxa-1,3,5,7,9,11-hexaazapentacyclo[5.5.3.$0^{2,6}$.$0^{4,10}$.$0^{8,12}$]pentadecane (**2**)

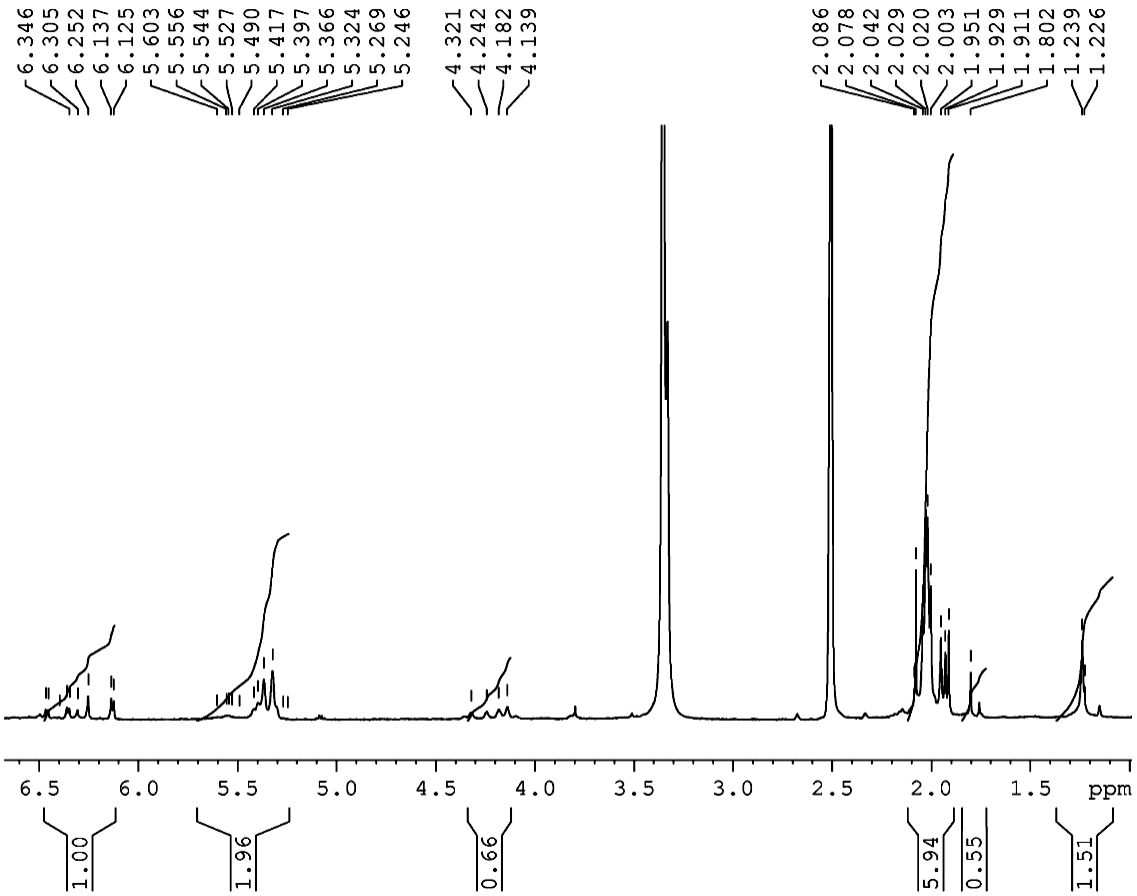

Figure S2 ^{1}H NMR 4-(1-hydroxyethyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **3a**

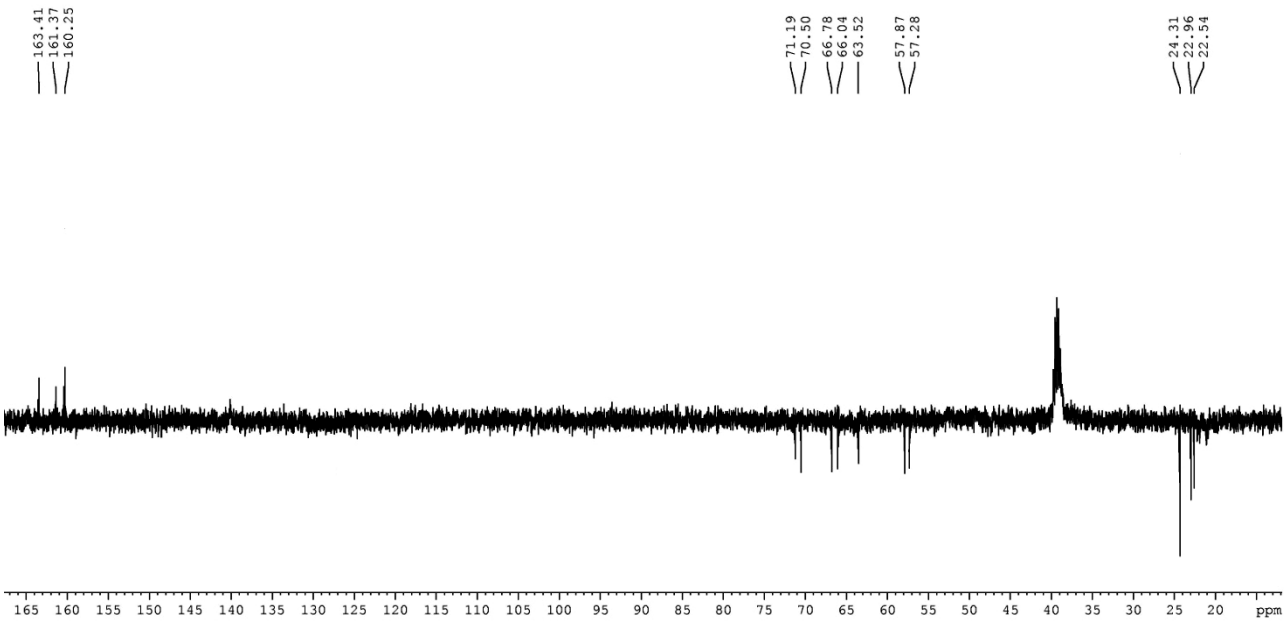

Figure S3 ^{13}C NMR 4-(1-hydroxyethyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **3a**

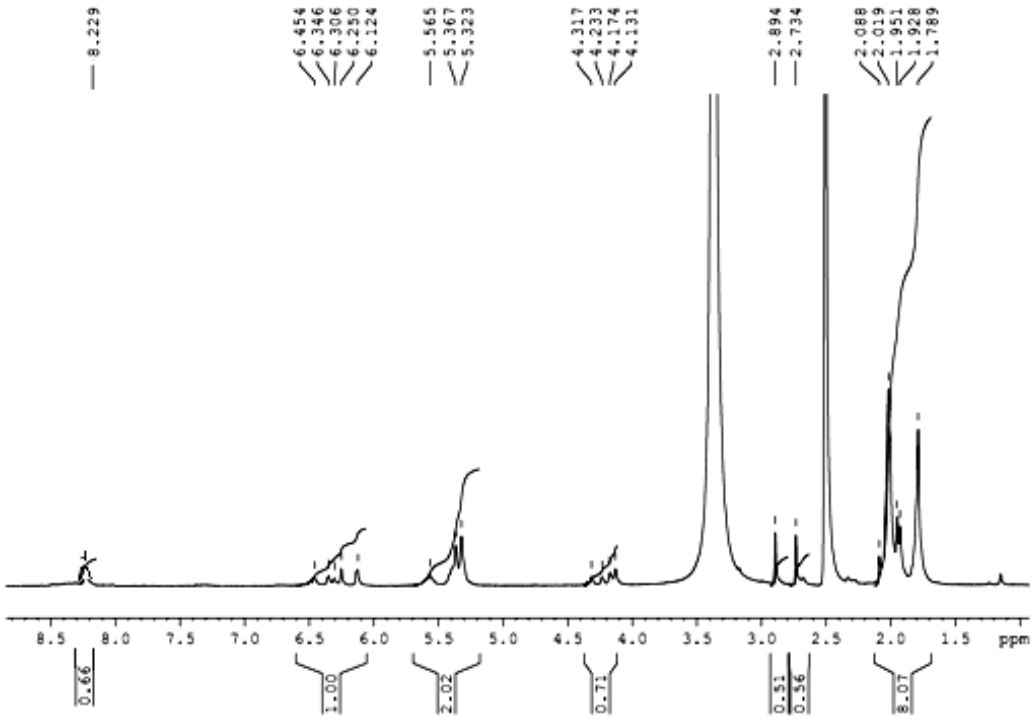

Figure S4 ^{1}H NMR 4-(1-hydroxypropyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **3b**

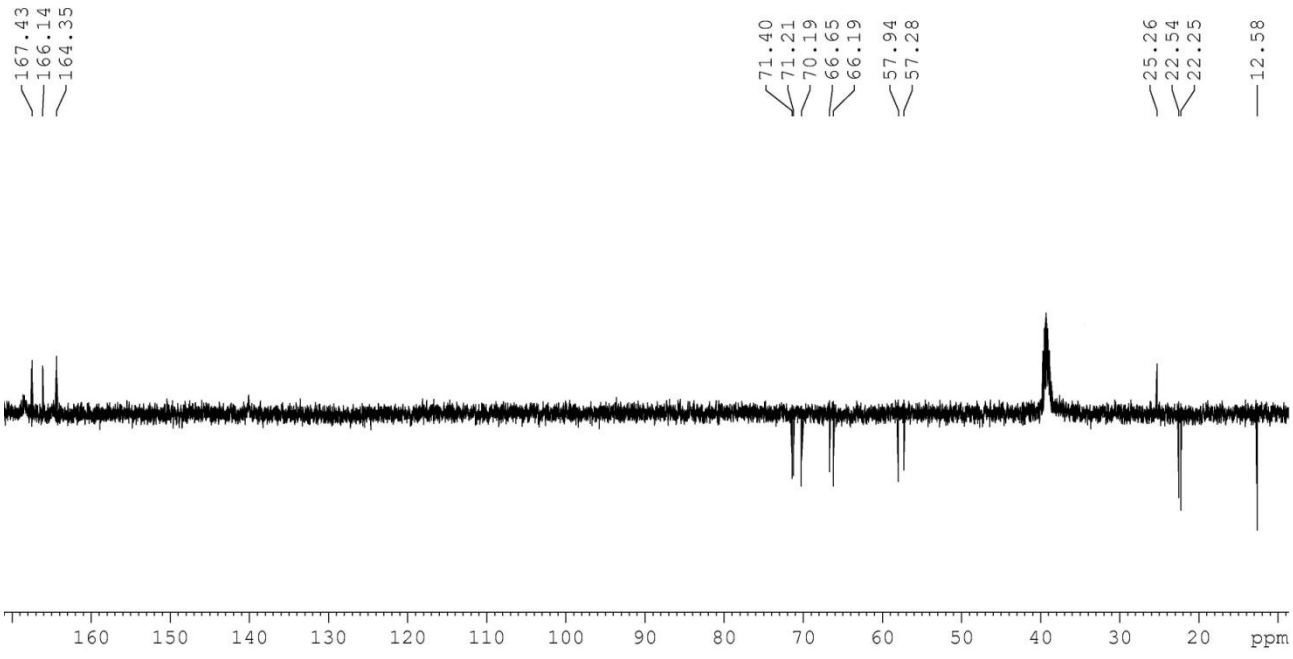

Figure S5 ^{13}C NMR 4-(1-hydroxypropyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **3b**

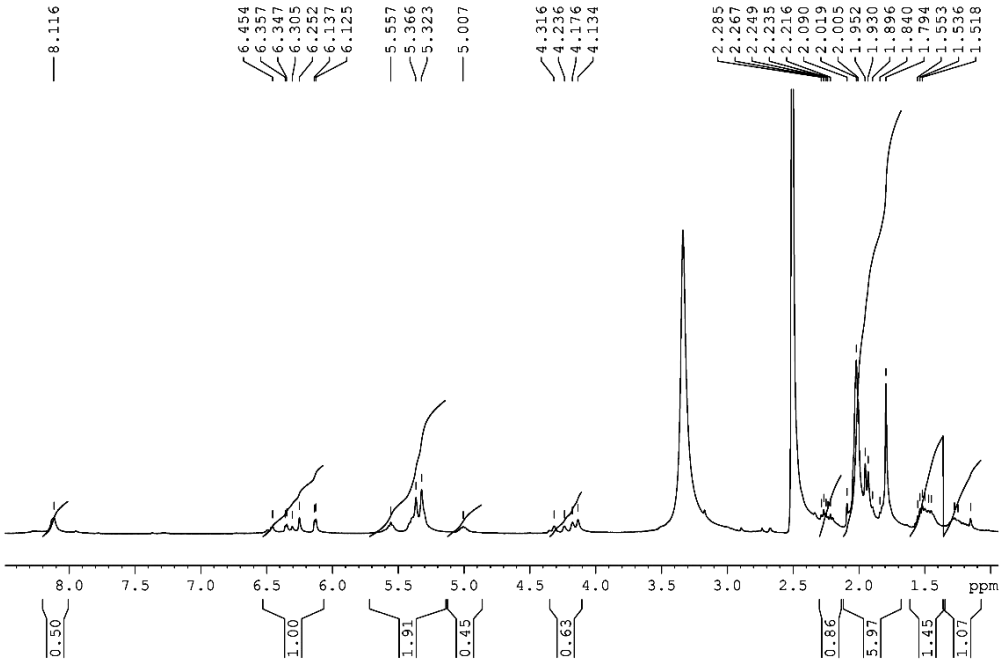

Figure S6 ^{1}H NMR 4-(1-hydroxybutyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **3c**

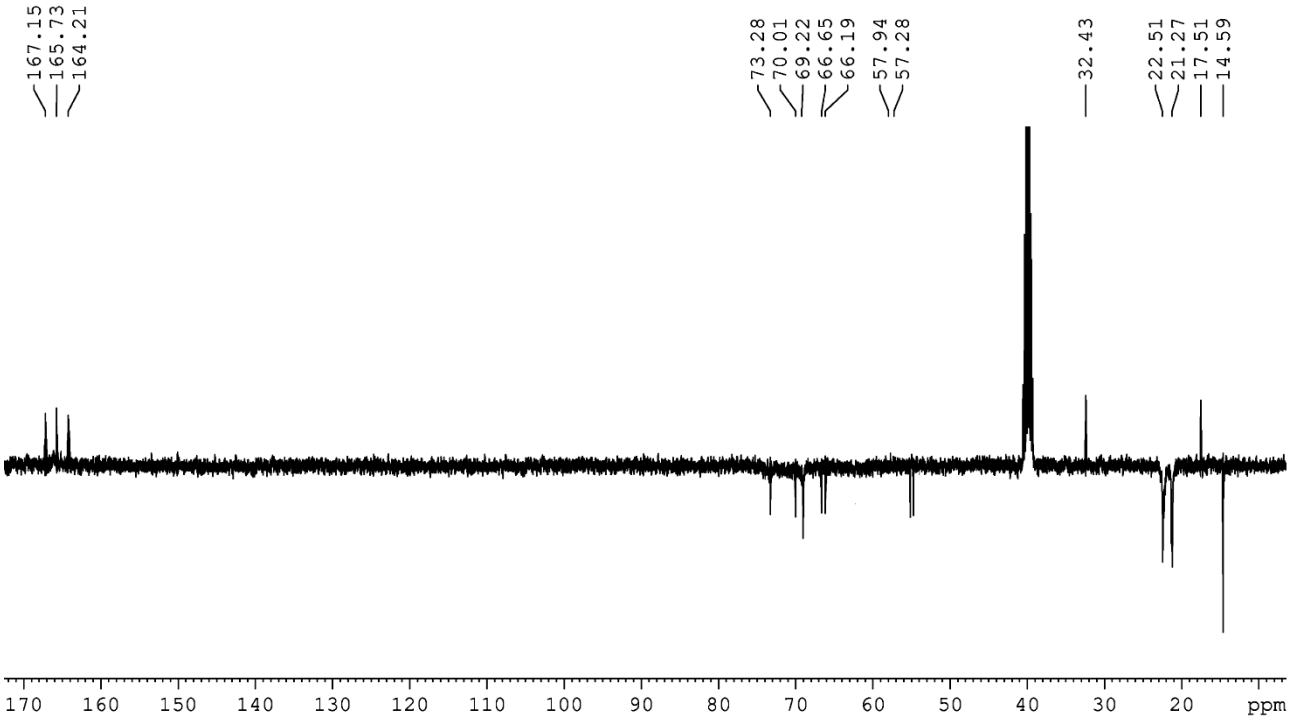

Figure S7 ^{13}C NMR 4-(1-hydroxybutyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **3c**

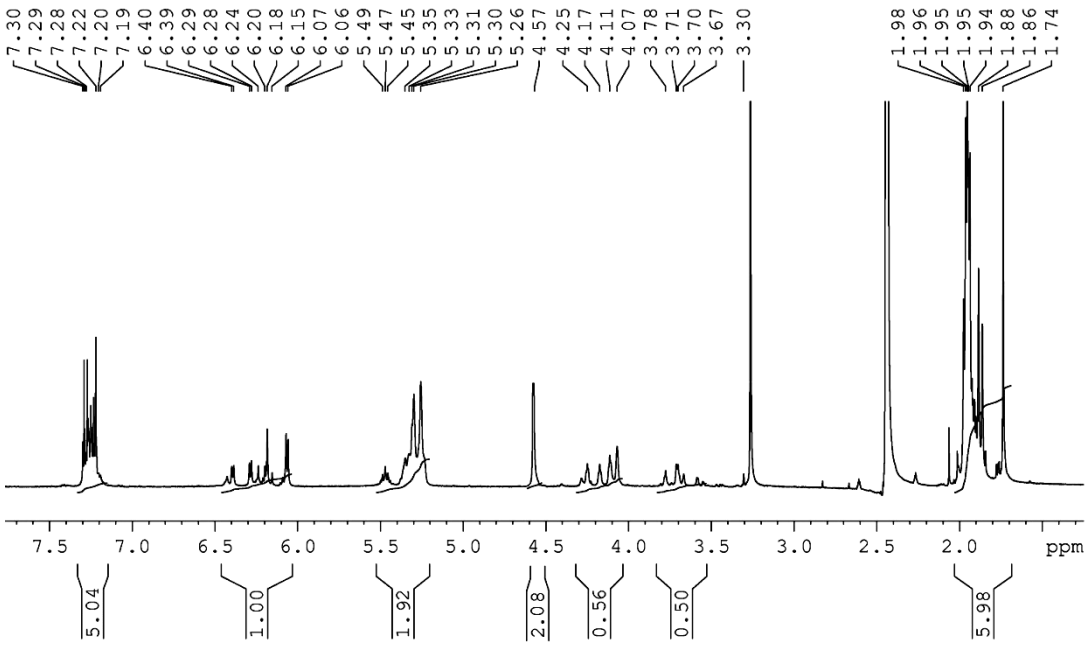

Figure S8 ^{1}H NMR 4-(*N*-benzylaminomethyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **4a**

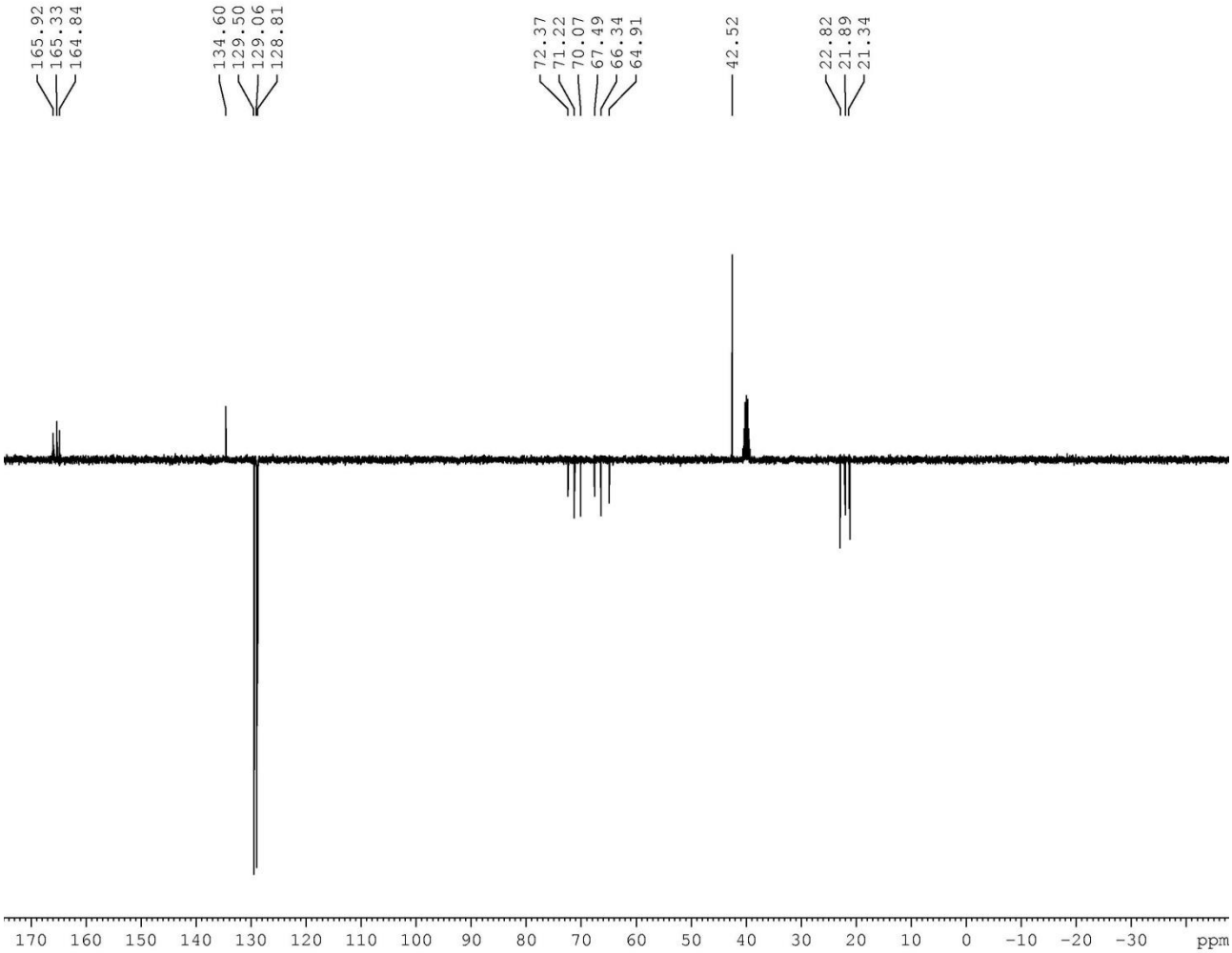

Figure S9 ^{13}C NMR 4-(*N*-benzylaminomethyl)-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **4a**

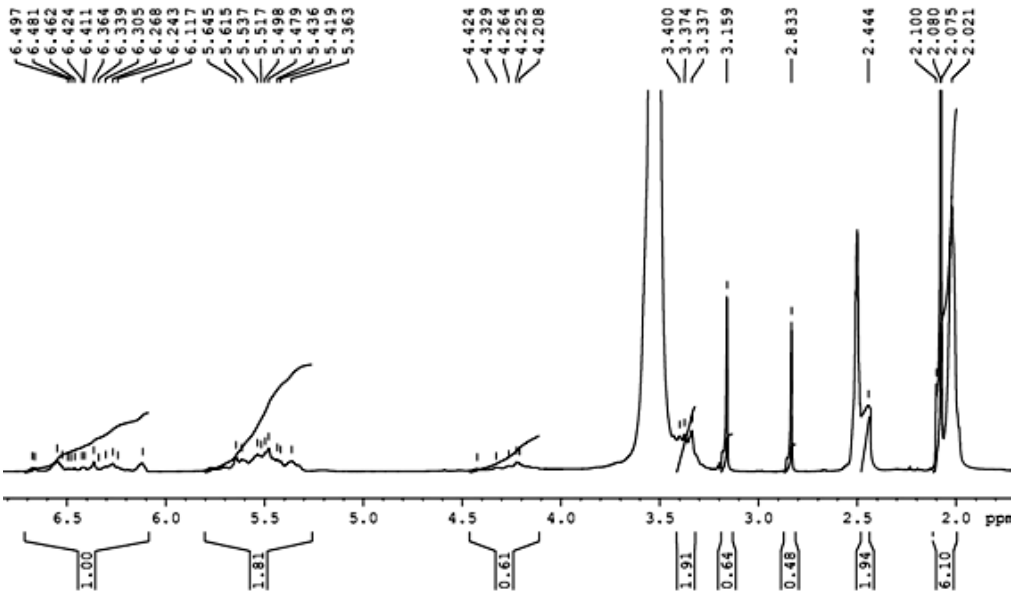

Figure S10 ^{1}H NMR 4-morpholinomethyl-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **4b**

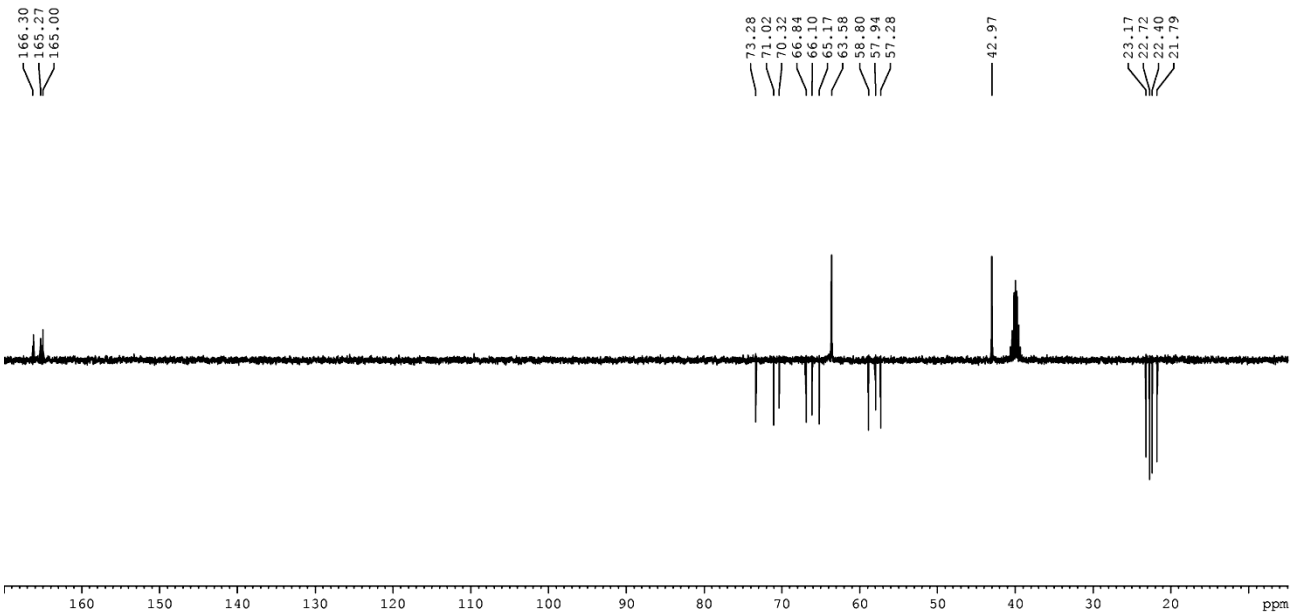

Figure S11 ^{13}C NMR 4-morpholinomethyl-2,6,8,12-tetraacetyl-2,4,6,8,10,12-hexaazaisowurtzitane **4b**