Electronic supplementary materials *Mendeleev Commun.*, 2014, **24**, 173−175

Regioselective synthesis of 2,8-disubstituted-1,5-diphenylglycolurils

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^{1}H and ^{13}C NMR were recorded on a Bruker Avance II 300, and TMS as internal standard. Mass spectra and HRMS (ESI) were recorded using Kratos MS-30 and Bruker micrOTOF II mass spectrometers respectively. Elemental analyses were performed on a Perkin Elmer 2400 Elemental CHN analyzer and Euro EA elemental Analizer.

*Synthesis of 1,6-bis(2-hydroxyethyl)-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione* **1a**.

Method 1: To the mixture of 1-(2-hydroxyethyl)urea **3a** (2.08 g, 0.02 mol) and benzil (2.10 g, 0.01 mol) in Pr^{i}OH (30 ml), HCl (0.6 ml, 35%) was added. The reaction mixture was refluxed with stirring for 2 h. Then the resulting mixture was kept for 72 h to give white precipitate. The precipitate (2.60 g, 68%) **1a** was filtered off and washed free of benzil with Et_2O.

Method 2: To the mixture of 1-(2-hydroxyethyl)urea **3a** (1.04 g, 0.01 mol) and 7-hydroxy-7,7a-diphenyltetrahydroimidazo[5,1-*b*]oxazol-5(6*H*)-one **7a** (2.96 g, 0.01 mol) in Pr^{i}OH (30 ml), HCl (0.6 ml, 35%) was added. The reaction mixture was refluxed with stirring for 20 min. Then the resulting mixture was kept for 72 h to give white precipitate. The precipitate of **1a** (3.55 g, 93%) was filtered off and washed free of benzil with Et_2O.

1a: mp 279–281 °C. ^{1}H NMR, δ, ppm.; *J*/Hz ($DMSOd_6$): 2.96-3.06 (m, 2 H, CH_2), 3.16-3.26 (m, 2 H, CH_2), 3.58-3.73 (m, 4 H, CH_2), 4.84 (t, *J* = 5.1, 2 H, OH), 6.79-7.89 (m, 2 H, Ph), 6.93-7.01 (m, 2 H, Ph), 6.02-7.16 (m, 6 H, Ph), 8.16 (s, 2 H, NH). ^{13}C NMR, δ, ppm.; ($DMSO-d_6$): 44.77, 59.42 (CH_2); 79.44, 89.79 (C-Ph); 127.01, 127.48, 127.93, 128.05, 128.46 (CH(Ph)); 133.42, 137.30 (C(Ph)); 160.28 (C=O). MS, m/z, (*I* %): 365[M^{+}-OH](5), 352(93), 323(12), 309(12), 293(14), 281(100), 251(59), 237(42), 222(20), 194(37).

*Synthesis of 1,6-bis(3-hydroxypropyl)-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]-imidazole-2,5(1*H*,3*H*)-dione* **1b**. To the mixture of **5** (1.55 g, 0.005 mol) and **3b** (0.59 g, 0.005 mmol) in MeOH (45 ml), HCl (0.6 ml) was added. The reaction mixture was refluxed with stirring for 8 h. Then the resulting mixture was kept at room temperature for 48 h to

give white precipitate. The precipitate was filtered off and washed free of benzil with Et_2O. The resulting precipitate (1.41 g, 69%) is **1b**.

1b: mp 244–245 °C. ^{1}H NMR, δ, ppm.; *J*/Hz ($DMSOd_6$): 1.74-1.93 (m, 4 H, 2 CH_2), 2.96-3.02 (m, 2 H, CH_2), 3.17-3.23 (m, 2 H, CH_2), 3.35-3.43 (q, 4 H, CH_2, *J* = 5.6), 4.44 (t, 2 H, 2 OH, *J* = 5.1), 6.74-7.82 (m, 2 H, Ph), 6.94-7.01 (m, 2 H, Ph), 7.04-7.15 (m, 6 H, Ph), 8.06 (s, 2 H, NH). ^{13}C NMR, δ, ppm.; ($DMSOd_6$): 32.77, 39.93, 58.71 (CH_2); 79.25, 90.24 (C-Ph), 127.15, 127.51, 127.94, 128.09, 128.15, 128.50 (CH(Ph)), 133.75, 137.54 (C(Ph)); 160.20 (C=O). MS, m/z, (*I* %): 410[M^+](10), 380(6), 335(19), 294(76), 250(19), 171(22), 162(48), 104(100).

*Synthesis of 1-(2-hydroxyethyl)-6-(3-hydroxypropyl)-3a,6a-diphenyltetrahydroimidazo-[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione* **1c.**

Method 1: To the mixture of 1-(3-hydroxypropyl)urea **3b** (1.18 g, 0.01 mol) and 7-hydroxy-7,7a-diphenyltetrahydroimidazo[5,1-*b*]oxazol-5(6*H*)-one **7a** (2.96 g, 0.01 mol) in Pr^{i}OH (30 ml), HCl (0.6 ml, 35%) was added. The reaction mixture was refluxed with stirring for 20 min. Then the resulting mixture was kept for 10 min to give white precipitate **7b** (25%). The next precipitate **1c** (1.62 g, 41%) was formed after 24 h.

Method 2: To the mixture of 1-(2-hydroxyethyl)urea **3a** (1.04 g, 0.01 mol) and (8*R**,8*aR**)-8-hydroxy-8,8a-diphenyltetrahydro-2*H*-imidazo[5,1-*b*][1,3]oxazin-6(7*H*)-one **7b** (3.10 g, 0.01 mol) in MeCN (180 ml), HCl (1 ml, 35%) was added. The reaction mixture was refluxed with stirring for 4 h. Then the reaction mixture was filtred off and filtrate was concentrated. Crude product was recrystallized from MeCN. Yield **1c** (3.55 g, 90%).

1c: mp 242-243 °C. ^{1}H NMR, δ, ppm.; *J*/Hz ($DMSOd_6$): 1.79-1.88 (m, 2 H, CH_2), 2.90-3.00 (m, H, CH_2), 3.06-3.22 (m, 2 H, CH_2), 3.25-3.43 (m, 5 H, CH_2), 3.67 (t, 2 H, OH, *J* = 6.9), 6.78-7.85 (m, 2 H, Ph), 6.97-7.02 (m, 2 H, Ph), 7.03-7.12 (m, 6 H, Ph), 8.01 (s, 2 H, NH), 8.12 (s, 2 H, NH). ^{13}C NMR, δ, ppm.; ($DMSOd_6$): 32.77, 40.33, 44.80, 58.69, 59.51 (CH_2); 79.39, 90.06 (C-Ph), 126.78, 127.15, 127.48, 127.65, 127.78, 127.99, 128.07, 128.16, 128.50 (CH(Ph)), 133.56, 137.40 (C(Ph)); 160.10, 160.47 (C=O). HRMS, m/z, found: 397.1868 $[M+H]^+$ (calcd for ($C_{21}H_{24}N_4O_4$ +H) 397.1870).

Synthesis of ureas **3a-c** *(general procedure).* An aqueous solution of the corresponding amino alcohol (0.05 mol) was heated to boiling and then KOCN (0.052 mol) was added in five portions to the gently refluxing solution. After the addition of all KOCN, the mixture was refluxed for 20 min, cooled to 20 °C, and treated with an equimolar amount (4.5 ml) of concentrated HCl to pH 1. Then the mixture was concentrated to dryness in vacuo. MeOH (20 mL) was added, and a precipitatee of KCl was filtered off. The filtrate was

concentrated in vacuo, (the product **3c** was formed from oily residue) the oily residue (for **3a,b**) was triturated with a MeOH-Et_2O mixture (1:2, 15 ml), and products **3a,b** that formed were filtered.

The physical data for compound **3a,b** are consistent with the literature data for these compounds synthesized by other methods.[20,21]

1-(2,3-Dihydroxypropyl)urea **3c**: yield 95%; mp 70–71 °C. ^{1}H NMR, δ, ppm.; J/Hz (DMSO-d_6): 2.86-2.95 (m, H, CH_2), 3.09-3.17 (m, H, CH_2), 3.21-3.26 (m, 2 H, CH_2), 3.27-3.47 (m, H, CH), 4.65 (br. s, H, OH), 4.80 (br. s, H, OH), 5.55 (s, 2 H, NH_2), 6.03 (br. s, H, NH). ^{13}C NMR, δ, ppm.; (DMSO-d_6): 42.56, 71.13 (CH_2); 63.46 (CH); 159.42 (C=O). HRMS, m/z, found: 157.0586 $[M+Na]^+$ (calcd for $NaC_4H_{10}N_2O_3$ 157.0584).

(7*RS*,7*aRS*)-*7-Methoxy-7,7a-diphenyltetrahydroimidazo[5,1*-b*]oxazol-5(6*H*)-one* **4**: HCl (0.6 ml, 35%) was added to the mixture of 1-(2-hydroxyethyl)urea **3a** (2.08 g, 0.02 mol) and benzil (2.10 g, 0.01 mol) in MeOH (25 ml). The reaction mixture was refluxed with stirring for 2 h. Then the resulting mixture was kept at room temperature for 24 h to give white precipitate. The precipitate was filtered and washed with Et_2O to remove excess benzil. The mixture of products was added into MeOH (20 ml) and refluxed for 1 min and then quickly filtered. The resulting precipitate (1.18 g, 38%) is compound **4**.

4: mp 250–252 °C. ^{1}H NMR, δ, ppm.; *J*/Hz (DMSO-d_6): 2.77-2.86 (m, 1 H, CH_2), 2.90 (s, 3 H, Me), 3.22-3.29 (m, 1 H, CH_2), 3.66-3.74 (m, 1 H, CH_2), 3.82-3.90 (m, 1 H, CH_2), 7.19-7.27 (m, 4 H, Ph), 7.33-7.40 (m, 6 H, Ph), 9.13 (s, 1 H, NH). ^{13}C NMR, δ, ppm.; (DMSO-d_6): 44.09, 63.53 (CH_2); 49.89 (Me); 91.35, 102.83 (C-Ph); 127.40, 127.62, 127.83, 128.01, 128.20, 128.40 (CH(Ph)); 135.01, 135.64 (C(Ph)); 163.73 (C=O). MS, m/z, (*I* %): 310$[M^+]$(3), 295(17), 175(26), 147(100), 117(69). HRMS, m/z, found: 333.1267 $[M+Na]^+$ (calcd for $NaC_{18}H_{18}N_2O_3$ 333.1267).

(8*RS*,8a*RS*)-*8-Methoxy-8,8a-diphenyltetrahydro-2*H-*imidazo[5,1*-b*][1,3]oxazin-6(7*H*)-one* **5.** HCl (0.6 ml, 35%) was added to the mixture of **3b** (2.36 g, 0.02 mol) and benzil (2.10 g, 0.01 mmol) in MeOH (45 ml). The mixture was refluxed with stirring for 2 h. Then the resulting mixture was kept at room temperature for 48 h to give white precipitate. The precipitate was filtered and washed with Et_2O to remove excess benzil, then it was recrystallized from MeOH (20 ml) to give **5** (2.13 g, 66%) and **1b** (0.2 g, 5%).

5: mp 230–232 °C. ^{1}H NMR, δ, ppm.; *J*/Hz (DMSOd_6): 1.10-1.19 (m, 1 H, CH_2), 1.55-1.76 (m, 1 H, CH_2), 2.79 (s, 3 H, Me), 2.80-2.90 (m, 1 H, CH_2), 3.23-3.39 (m, 1 H, CH_2), 3.47-3.51 (m, 1 H, CH_2), 3.72-3.83 (m, 1 H, CH_2), 7.15-7.24 (m, 2 H, Ph), 7.25-7.62 (m, 8 H, Ph), 8.90 (s, 1 H, NH). ^{13}C NMR, δ, ppm.; (DMSO-d_6): 23.54, 37.11, 61.45 (CH_2); 49.38 (Me);

92.75, 95.13 (C-Ph); 127.37, 127.76, 128.21, 128.62 (CH(Ph)); 134.00, 134.80 (C(Ph)); 160.33 (C=O). HRMS, m/z, found: 325.1553 $[M+H]^+$ (calcd for $H+C_{19}H_{20}N_2O_3$ 325.1552).

(3*RS*,8*RS*,8a*RS*)-*3-Hydroxy-8-methoxy-8,8a-diphenyltetrahydro-2*H-*imidazo[5,1-*b*][1,3]oxazin-6(7*H*)-one* **6.** HCl (0.6 ml, 35%) was added to the mixture of **3c** (2.68 g, 0.02 mol) and benzil (2.10 g, 0.01 mmol) in MeOH (25 ml). The reaction mixture was refluxed with stirred for 2 h. Then the resulting mixture was kept at room temperature for 48 h to give white precipitate. The precipitate was filtered and washed with Et_2O to remove excess benzil, then it was recrystallized from MeCN (20 ml) to give product **6** (2.07 g, 61%).

6: mp 252–253 °C. ^{1}H NMR, δ, ppm.; *J*/Hz (DMSO-d_6): 2.43-2.49 (m, 1 H, CH_2), 2.79 (s, 3 H, Me), 2.83-2.90 (m, 1 H, CH_2), 3.40-3.54 (m, 2 H, CH+CH_2), 3.83-3.93 (m, 1 H, CH_2), 5.03 (d, 1 H, OH, *J* = 5.1), 6.86-7.01 (m, 1 H, Ph), 7.13-7.22 (m, 2 H, Ph), 7.32-7.53 (m, 7 H, Ph), 8.90 (s, 1 H, NH). ^{13}C NMR, δ, ppm.; (DMSO-d_6): 44.00, 66.27 (CH_2); 49.47 (Me); 60.33 (CH), 92.45, 94.43 (C-Ph); 127.47, 127.85, 128.36, 128.52, 130.45 (CH(Ph)); 133.34, 134.67 (C(Ph)); 160.27 (C=O). HRMS, m/z, found: 363.1316 $[M+Na]^+$ (calcd for $NaC_{19}H_{20}N_2O_4$ 363.1315).

*7-Hydroxy-7,7a-diphenyltetrahydroimidazo[5,1-*b*]oxazol-5(6*H*)-one* **7a.** To the suspension of 1-(2-hydroxyethyl)-4,5-diphenyl-1*H*-imidazol-2(3*H*)-one **9** (5.60 g, 0.02 mol) in MeCN (40 ml), HNO_3 (6.4 ml, 60%, 0.08 mol) was added dropwise. The reaction mixture was stirred at room temperature for 5 min. Then the resulting white precipitate was filtered and washed with Et_2O to remove excess benzil. The resulting precipitate is **7a** (5.33 g, 90%).

7a: mp 204–205 °C. ^{1}H NMR, δ, ppm.; *J*/Hz (DMSO-d_6): 3.33-3.43 (m, H, CH_2), 3.52-3.62 (m, H, CH_2), 3.90-4.06 (m, 2 H, CH_2), 6.42 (s, H, OH), 7.00-7.14 (m, 10 H, Ph), 8.46 (s, 1 H, NH). ^{13}C NMR, δ, ppm.; (DMSO-d_6): 44.14, 45.02, 63.80, 64.26 (CH_2); 86.36, 88.61 (C-Ph); 125.36, 126.31, 126.56, 126.97, 127.24, 127.27, 127.48, 127.56, 127.65, 127.75, 128.86, 130.18 (CH(Ph)); 136.27, 136.92, 138.94, 140.99 (C(Ph)); 162.35, 163.47 (C=O). HRMS, m/z, found: 297.1236 $[M+H]^+$ (calcd for $H+C_{17}H_{16}N_2O_3$ 297.1234).

(8*RS*,8a*RS*)-*8-Hydroxy-8,8a-diphenyltetrahydro-2*H-*imidazo[5,1-*b*][1,3]oxazin-6(7*H*)-one* ***7*b.** To the mixture of **3b** (2.36 g, 0.02 mol) and benzil (2.10 g, 0.01 mmol) in Pr^{i}OH (30 ml), HCl (0.6 ml, 35%) was added. The reaction mixture was refluxed with stirring for 2 h. Then the resulting mixture was cooled to room temperature and the white solid was filtered and washed with Et_2O to remove excess benzil to give **7b** (1.96 g, 63%).

7b: mp 269–271 °C. ^{1}H NMR, δ, ppm.; *J*/Hz (DMSO-d_6): 1.20-1.33 (m, 1H, CH_2), 1.72-1.92 (m, 1H, CH_2), 2.75-2.88 (m, 1H, CH_2), 3.50-3.63 (m, 1H, CH_2), 3.79-3.90 (m, 1H, CH_2), 3.92-4.08 (m, 1H, CH_2), 5.89-5.97 (br. s, 1H, OH), 6.85-7.15 (m, 8H, Ph), 7.45 (s, 2H, Ph), 8.05 (s, 1H, NH). ^{13}C NMR, δ, ppm.; (DMSO-d_6): 23.39 (CH_2) , 36.83 (CH_2), 62.64 (CH_2); 89.46,

93.84 (C-Ph); 126.58, 126.87, 127.02, 127.17, 128.59, 129.52 (Ph); 134.92, 140.94 (C(Ph)); 159.66 (C=O). HRMS, m/z, found: 311.1394 $[M+H]^+$ (calcd for $H+C_{18}H_{18}N_2O_3$ 311.1390).

*3,8-Dihydroxy-8,8a-diphenyltetrahydro-2*H-*imidazo[5,1*-b*][1,3]oxazin-6(7*H*)-one* **7c:** To the mixture of **3c** (2.68 g, 0.02 mol) and benzil (2.10 g, 0.01 mmol) in Pr^{i}OH (30 ml), HCl (0.6 ml) was added. The reaction mixture was refluxed with stirring for 2 h. The resulting mixture was evaporated at reduced pressure, then $CHCl_3$ (7 ml) was added and the white precipitate was filtred. The resulting precipitate is compound **7c** (2.12 g, 65%).

7c: mp 244–246 °C. ^{1}H NMR, δ, ppm.; *J*/Hz (DMSO-d_6): 2.92 (d, 1H, CH_2, *J* = 13.7 for one of diastereomers), 2.96 – 3.80 (m, 8H, 2CH+3CH_2), 3.88 (d, 1H, CH_2, *J* = 14.1 for other of diastereomers), 5.72 (br.s, 1H, OH for one of diastereomers), 6.62 (br.s, 1H, OH for other of diastereomers), 6.83 – 7.12 (m, 8H, Ph), 7.23 – 7.43 (m, 12H, Ph), 7.84 (s, H, OH for one of diastereomers), 7.93 (s, H, OH for other of diastereomers), 8.19 (s, H, NH for one of diastereomers), 8.26 (s, H, NH for other of diastereomers). HRMS, m/z, found: 327.1339 $[M+H]^+$ (calcd for $H+C_{18}H_{18}N_2O_4$ 327.1339).

*8,8a-Diphenyl-3,4-dihydro-2*H-*imidazo[5,1*-b*][1,3]oxazin-6(8a*H*)-one* **8b.** Compound **7b** was heated to boiling in an NMR ampoule in DMSO-d_6 for 3 minutes.

8b: ^{1}H NMR, δ, ppm.; *J*/Hz (DMSO-d_6): 1.50-1.62 (m, 1 H, CH_2), 1.64-1.85 (m, 1 H, CH_2), 2.87-2.97 (m, 1 H, CH_2), 3.95-4.18 (m, 2 H, CH_2), 4.10-4.22 (m, 1 H, CH_2), 7.32-7.39 (m, 1 H, Ph), 7.40-7.49 (m, 6 H, Ph), 7.55 (t, 1 H, Ph, *J* = 7.1), 8.06 (d, 2 H, Ph, *J* = 7.6). ^{13}C NMR, δ, ppm.; (DMSO-d_6): 24.26, 36.25, 63.05 (CH_2); 93.88 (C-Ph); 126.50, 126.79, 127.56, 127.17, 128.48, 128.80, 129.26, 129.44 (Ph); 133.07, 133.52 (C(Ph)); 163.44 (C=O); 185.26 (C=N).

*3-Hydroxy-8,8a-diphenyl-3,4-dihydro-2*H-*imidazo[5,1*-b*][1,3]oxazin-6(8a*H*)-one* **8c.** Compound **7c** was heated to boiling in an NMR ampoule in DMSO-d_6 for 3 min.

8c: ^{1}H NMR, δ, ppm.; *J*/Hz (DMSO-d_6): 3.02 (d, 1 H, CH_2, *J* = 13.5), 3.63-3.68 (m, 1 H, CH_2) 3.93 (d, 1 H, CH_2, *J* = 13.9), , 4.00-4.22 (m, H, CH+CH_2), 5.43 (d, 1 H, OH, *J* = 4.7), 7.42-7.51 (m, 7 H, Ph), 7.56 (t, 1 H, Ph, *J* = 6.8), 8.07 (d, 2 H, Ph, *J* = 7.5).

*1-(2-Hydroxyethyl)-4,5-diphenyl-1*H-*imidazol-2(3*H*)-one* **9**. A mixture of 1-(2-hydroxyethyl)urea **3a** (8.32 g, 0.08 mol) and benzoin (4.24 g, 0.02 mol) in ethylene glycol (30 ml) was heated at 170 °C for 1 h. After cooling to room temperature, the product was treated with $CHCl_3$ (10 ml) and water (40 ml), then the organic solution of **9** was separated and concentrated *in vacuo*. The pale yellow solid was recrystallized from MeCN to give the product **9** (4.2 g, 75%).

9: mp 230–232 °C. ^{1}H NMR, δ, ppm.; J/Hz (DMSO-d_6): 3.27-3.50 (m, 4 H, CH_2), 4.79 (s, H, OH), 7.03-7.24 (m, 5 H, Ph), 7.3-7.54 (m, 5 H, Ph), 10.78 (s, H, NH). ^{13}C NMR, δ, ppm.;

(DMSO-d_6): 42.92, 58.67 (CH_2); 117.06, 120.77, 125.33, 126.35, 128.29, 128.79, 128.97, 129.74, 130.92 (Ph-C=C-Ph); 153.23 (C=O).

*5-Hydroxy-1-(2-hydroxyethyl)-4,5-diphenyl-1*H-*imidazol-2(5*H*)-one* **10.** To the suspension of compound **9** (5.60 g, 0.02 mol) in MeCN (40 ml), HNO_3 (3.2 ml, 60%, 0.04 mol) was added dropwise. The reaction mixture was stirred at room temperature for 5 min. Then the mixture was diluted with H_2O (20 ml), the resulting white precipitate was filtered and washed with Et_2O to remove excess benzil. The resulting precipitate is **10** (3.32 g, 56%).

10: mp 225–227 °C. ^{1}H NMR, δ, ppm.; *J*/Hz (DMSO-d_6): 2.82-2.93 (m, 2 H, CH_2), 3.10-3.20 (m, 1 H, CH_2), 3.23-3.33 (m, 1 H, CH_2), 4.68 (br.s., 1 H, OH), 7.31-7.49 (m, 7 H, Ph), 7.54 (t, 1 H, Ph, *J* = 7.2), 7.73 (s, 1 H, OH), 7.99 (d, 1 H, Ph, *J* = 7.2). ^{13}C NMR, δ, ppm.; (DMSO-d_6): 41.12, 58.37 (CH_2); 92.70 (C-Ph); 125.15, 126.99, 127.93, 128.71, 128.97, 129.64 (CH(Ph)); 133.06, 137.02 (C(Ph)); 163.78 (C=O); 186.24 (C=N HRMS, m/z, found: 297.1236 $[M+H]^+$ (calcd for $H+C_{17}H_{16}N_2O_3$ 297.1234).

The diffraction patterns of the samples (**1a**, **1b**, **4**, **5**) were recorded using a PANalytical EMPYREAN diffractometer with Cu*K*α1 radiation (hybrid Ge{111} monochromator on the primary beam) and a PIXcell position sensitive detector. The measurements were performed in the reflection mode using $\theta/2\theta$ scanning with 0.013° step with respect to 2θ. The measurement range is 5 – 60° with respect to 2θ.

The interplanar spacings and the integral intensities used to refine the unit cell parameters were calculated using the profile analysis data for the experimental diffraction patterns (Rietveld method).The indices on the diffraction patterns were assigned using ITO and TREOR software.

All calculations for refinement of diffraction patterns and determination and refinement of the unit cell parameters were carried out using the HighScore Plus software package, Version:3.0.t (3.0.5), Date 30-01-2012. Produced by: PANalytical B.V. Amelo, The Netherlands.

The experimental diffraction patterns, the unit cell parameters and sets of interplanar spacings with intensities obtained for compounds (**1a, 1b, 4, 5**) have been deposited to the PDF database of the International Centre for Diffraction Data (ICDD).

Analysis of experimental powder diffraction patterns for compounds **1a,b, 4** and **5** shows that the samples studied had a single-phase nature. The unit cell parameters obtained for the compounds match those for the single crystal experiment, whereas the observed deviations are due to the thermal expansion of the crystal.

Table S1 Space groups, unit cell parameters and characteristics of the investigated verification phases **1a,b;4,5.**

	1a	**1b**	**4**	**5**
Compound	**$C_{22}H_{26}N_4O_4$**	**$C_{20}H_{22}N_4O_4$**	**$C_{20}H_{18}N_4O_4$**	**$C_{19}H_{20}N_2O_3$**
Space group, Z	**P-1**, Z=2	**$P2_1/n$**, Z=4	**P-1**, Z=6	**C2/c**, Z=8
a, (Å)	8.506(2)	9.255(1)	14.315(2)	19.850(2)
b, (Å)	9.023(2)	14.323(2)	18.479(3)	6.859(1)
c, (Å)	14.112(3)	14.264(2)	9.853(5)	26.425(4)
α, (^{o})	76.86(2)	90.0	91.27(2)	90.0
β, (^{o})	97.38(2)	99.52(2)	90.84(2)	102.97(2)
γ, (^{o})	101.57(2)	90.0	76.00(2)	90.0
V(Å^3)	1028.88	1864.79	2528.23	3506.01
Number unique reflections	143	52	73	79
Snyder's FOM	47.16	24.21	15.91	16.05

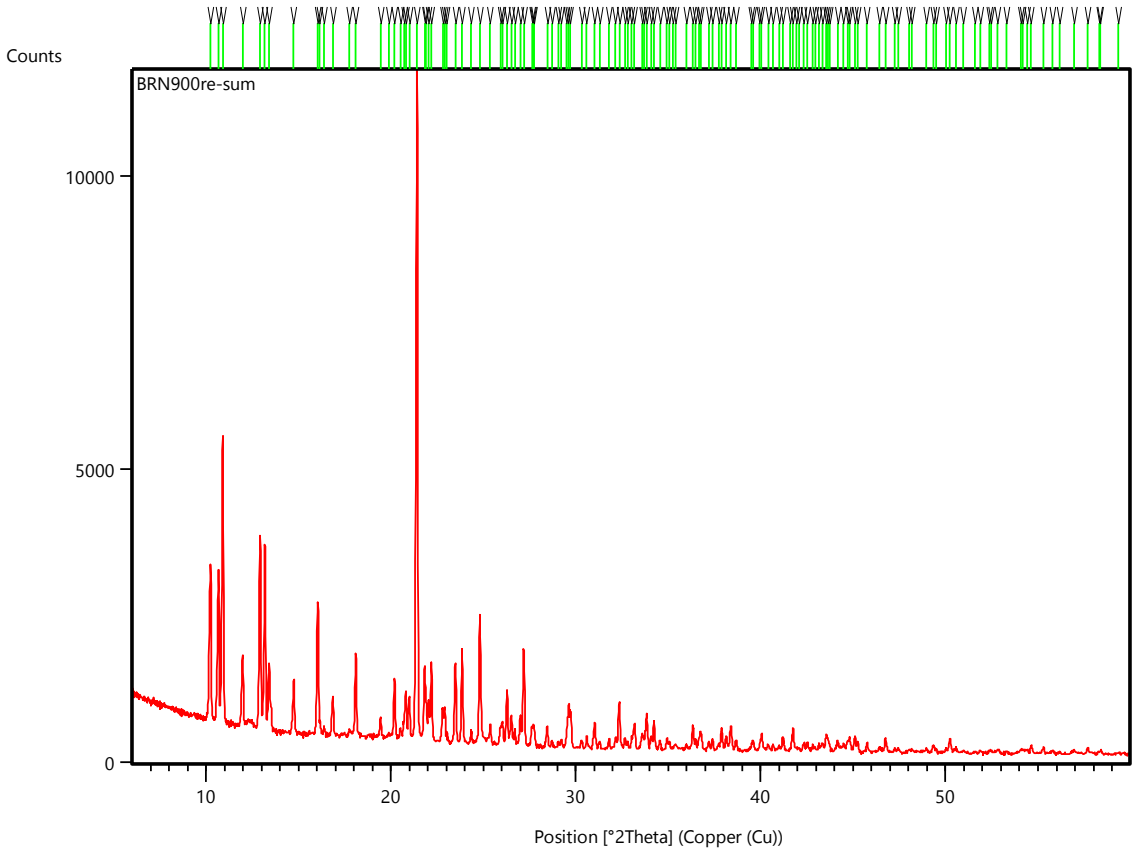


Figure S1 Powder diffraction pattern of (**1a**).

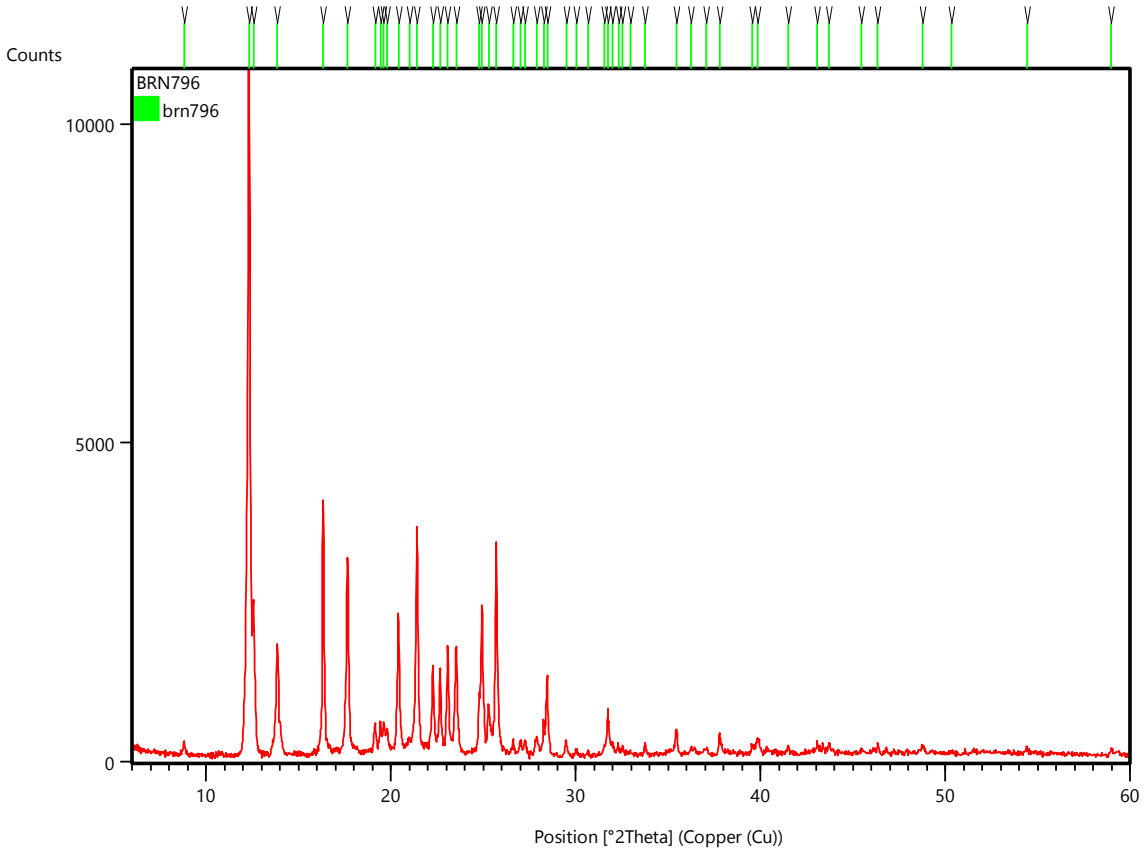


Figure S2 Powder diffraction pattern of (**1b**).

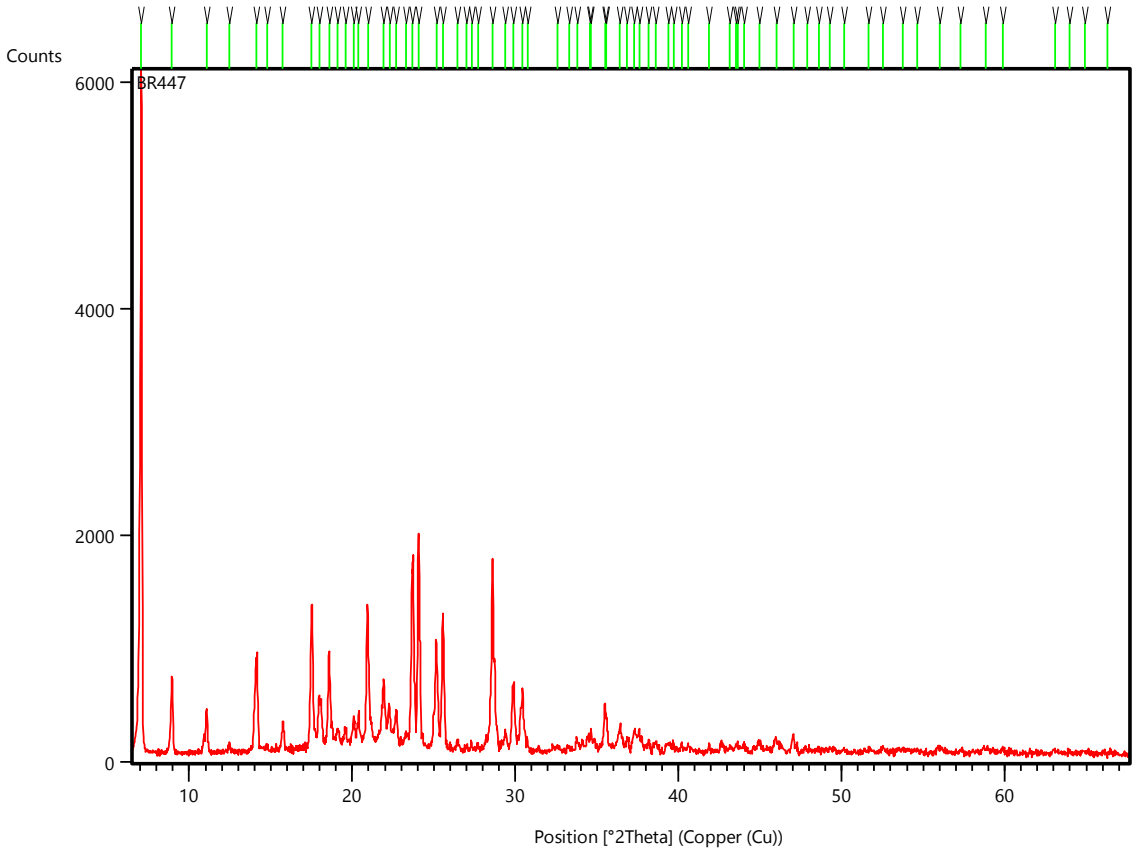


Figure S3 Powder diffraction pattern of (**4**).

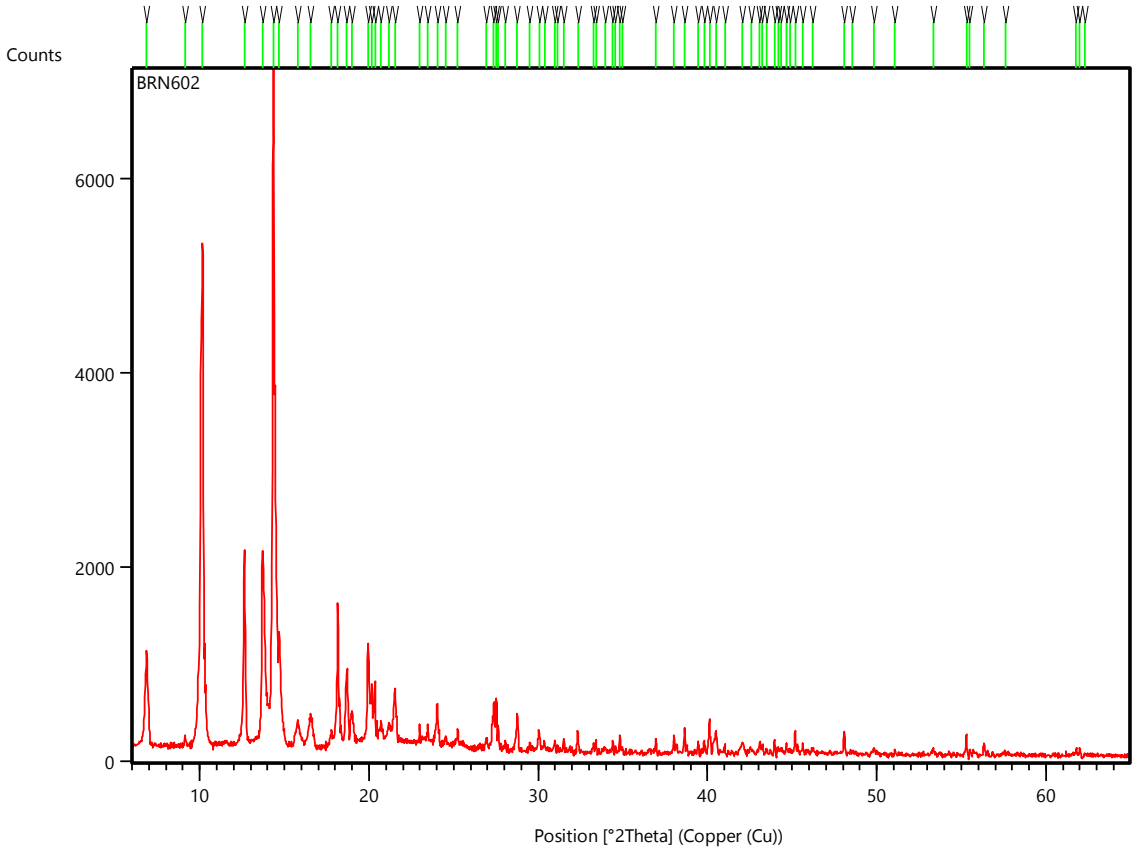


Figure S4 Powder diffraction pattern of (**5**).

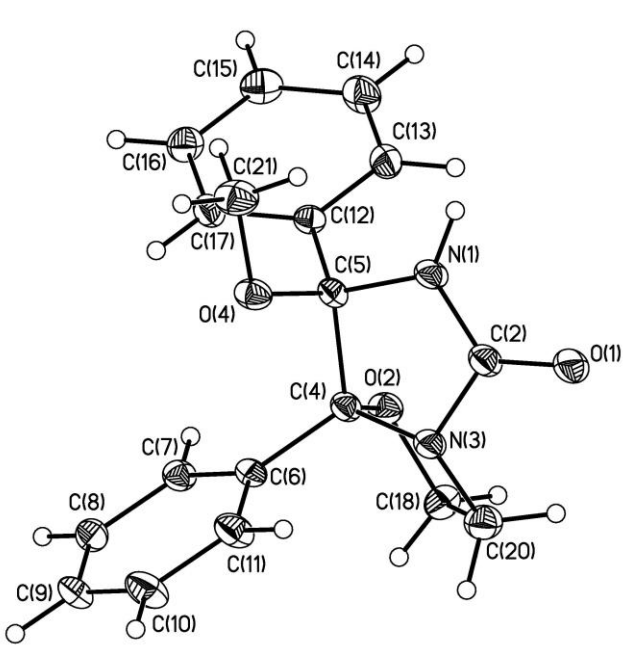
X-ray crystallography

X-ray diffraction experiments for **1a,b**, **4-6** and **7b** were carried out with a APEX2 DUO CCD diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å, ω-scans) at 100K (for **1b**, **4** and **5**) and 120K (for **1a**, **6** and **7b**). The structures were solved by direct method and refined by the full-matrix least-squares against F^2 in anisotropic approximation for non-hydrogen atoms. Hydrogen atom of NH and OH groups were found in difference Fourier synthesis; the H(C) atom positions were calculated. All hydrogen atoms were refined in isotropic approximation in riding model. Crystal data and structure refinement parameters for **1a,b**, **4-6** and **7b** are given in Table S1. All calculations were performed using the SHELXTL software [G. M. Sheldrick, *Acta Crystallogr. A*, 2008, **64**, 112].

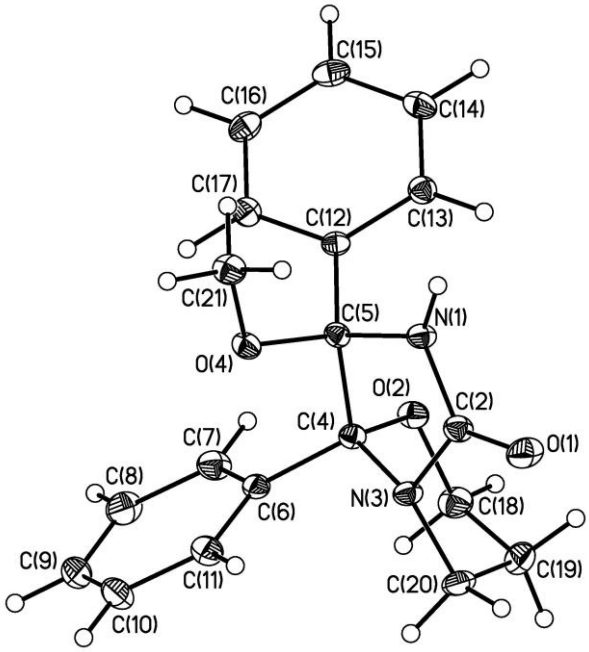
CCDC 967848−967853 contain the supplementary crystallographic data for **1a,b**, **4-6** and **7b**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

Table S2 Crystal data and structure refinement parameters for **1a,b**, **4-6** and **7b**.

	1a	**1b**	**4**	**5**	**6**	**7b**
Empirical formula	$C_{20}H_{22}N_4O_4$	$C_{22}H_{26}N_4O_4$	$C_{18}H_{18}N_2O_3$	$C_{19}H_{20}N_2O_3$	$C_{40}H_{43}N_5O_8$	$C_{20}H_{24}N_2O_4S$
Formula weight	382.42	410.47	310.34	324.37	721.79	388.47
T, K	120	100	100	100	120	120
Crystal system	Monoclinic	Triclinic	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1/n$	P-1	C2/c	C2/c	$P2_1/c$	P-1
Z	4	2	8	8	4	2
a, Å	9.2052(10)	8.4793(6)	28.7227(14)	19.6570(10)	16.1542(4)	8.4498(8)
b, Å	14.2576(16)	8.9672(6)	6.8499(3)	6.7384(3)	7.7292(2)	9.6902(9)
c, Å	14.2032(16)	14.0818(10)	17.6376(9)	26.1157(13)	28.6109(7)	12.0607(11)
α, °	90.00	76.7080(10)	90.00	90.00	90.00	85.198(2)
β, °	99.436(2)	83.0050(10)	118.0080(10)	102.9760(10)	95.1510(10)	85.353(2)
γ, °	90.00	78.9000(10)	90.00	90.00	90.00	70.533(2)
V, $Å^3$	1838.9(4)	1019.17(12)	3063.7(3)	3370.9(3)	3557.90(15)	926.33(15)
D_{calc} (g cm^{-1})	1.381	1.338	1.346	1.278	1.347	1.393
Linear absorption, μ (cm^{-1})	0.98	0.94	0.93	0.87	7.78	2.04
F(000)	808	436	1312	1376	1528	412
$2\theta_{max}$, °	56	58	56	58	129	57
Reflections measured	18496	16904	16837	19301	35301	10235
Independent reflections	4440	5428	3699	4477	5833	4902
Observed reflections [$I > 2\sigma(I)$]	2920	4383	3354	3613	5651	3538
Parameters	253	271	208	217	482	244
R1	0.0550	0.0383	0.0466	0.0382	0.0532	0.0531
wR2	0.1422	0.1014	0.1467	0.1038	0.1958	0.1373
GOF	1.000	1.007	1.091	1.006	1.531	1.004
$\Delta\rho_{max}$/ $\Delta\rho_{min}$ (e $Å^{-3}$)	0.333/-0.254	0.388/-0.246	0.648/-0.379	0.390/-0.221	0.392/-0.319	0.808/-0.328



4



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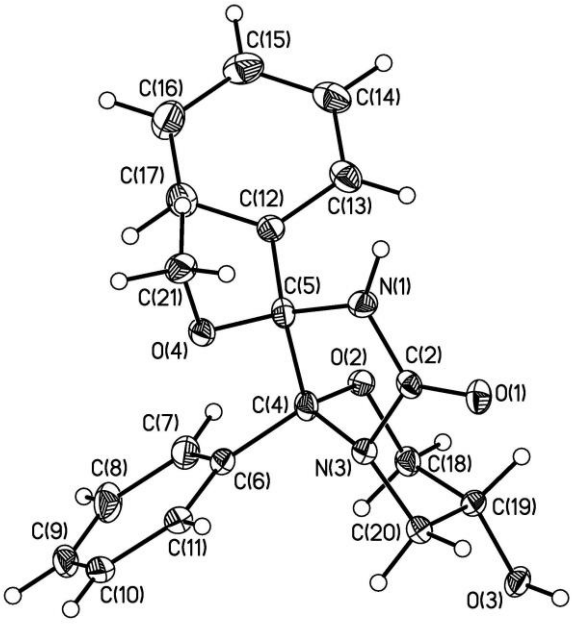
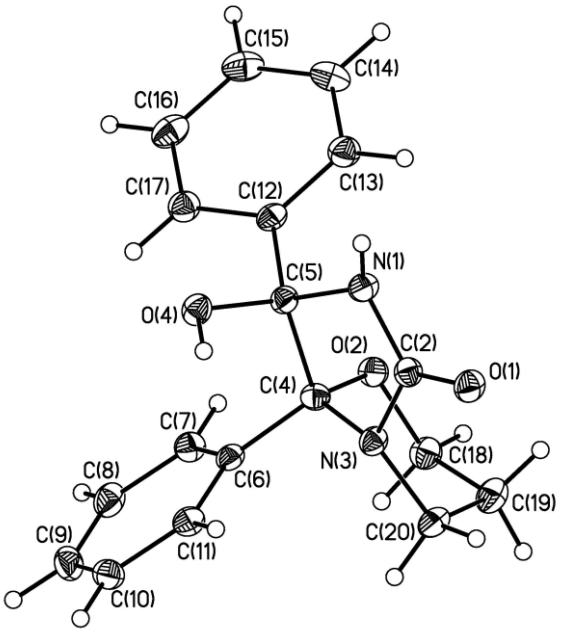


6



7b

Figure S5 General view of the compounds **4-6** and **7b** in representation of atoms *via* thermal ellipsoids at 50% probability level. A second independent molecule of the product and a solvate acetonitrile molecule in 6 and a solvate DMSO molecule in **7b** are not shown for clarity.