SUPPORTING INFORMATION

Synthesis, X-Ray Crystal Structures, Biological Evaluation and Molecular docking Studies of a Series of Barbiturate Derivatives

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Contents:

5. Experimental section

*5.1. General Procedure for Aldol Condensation Michael Addition for the Synthesis of **4** and **5.** (GP1)*

A mixture of aldehyde **3** (1.5mmol), **1** and **2** (3 mmol) as well as Et_2NH (1.5 mmol, 155 μL) in 3 mL of degassed H_2O (bubbling nitrogen through the water) was stirred at room temperature for 1–5 h until TLC showed complete disappearance of the reactants. The precipitate was removed by filtration and washed with ether (3 × 20 mL). The solid was dried to afford pure products **4** and **5.**

4-(bis(6-Hydroxy-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzaldehyde Diethylaminium Salt **(4a)**

Pure product **4a** was obtained according to **GP1** as colorless crystal (1.5 g, 2.76 mmol, 92%). IR (cm^{-1}): 3450, 3000, 2872, 1670, 1582, 1510, 1466, 1384, 1339; ^{1}H-NMR ($CDCl_3$, 400 MHz) 17.58 (s, 1H, OH), 9.90(s, 1H, CHO), 7.73 (d, 2H, J = 8.0 Hz, Ph), 7.29 (d, 2H, J = 8.0 Hz, Ph), 5.93 (s, 1H, benzyl-H), 3.33 (s, 12H, $4CH_3$), 3.06 (q, 4H, J = 7.3 Hz, CH_2CH_3), 1.27 (t, 6H, J = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 192.2, 165.3, 164.4, 151.7, 150.3, 134.3, 129.9, 127.3, 91.7, 42.2, 35.1, 29.0, 28.7, 11.5; LC/MS (ESI): 501.53 $[M]^+$; Anal. for $C_{24}H_{31}N_5O_7$; Calcd: C, 57.48; H, 6.23; N, 13.96; Found: C, 57.50; H, 6.25; N, 14.00.

*5,5'-(3-Tolylmethylene)bis(1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione) Diethylaminium Salt **(4b)***

4b was prepared from 1,3-dimethylbarbituric acid **1a**, and *m*-tolualdehyde according to the general procedure (**GP1**) yielding rose-colored crystalline materials. (1.41 g, 2.91

mmol, 97%). m.p.: 135 °C; IR (KBr, cm^{-1}): 3455, 3201, 2988, 1693, 1667, 1611, 1573, 1443; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 17.62 (s, 1H, OH), 7.10 (t, 1H, J = 7.3 Hz, Ph), 6.92 (d, 1H, J = 7.3 Hz, Ph), 6.88 (d, 1H, J = 7.3 Hz, Ph), 5.82 (s, 1H, benzyl-H), 3.32 (s, 12H, $4CH_3$), 3.01 (q, 4H, J = 7.3 Hz, CH_2CH_3), 2.25 (s, 3H, CH_3), 1.26 (t, 6H, J = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.3, 164.4, 151.8, 141.7, 137.4, 127.9, 127.1, 126.4, 123.6, 92.1, 42.0, 34.4, 28.9, 28.6, 21.8, 11.4; LC/MS (ESI): 487$[M]^+$; Anal. for $C_{24}H_{35}N_5O_6$; Calcd: C, 59.12; H, 6.82; N, 14.36; Found: C, 59.13; H, 6.81; N, 14.35.

5,5'-((4-Nitrophenyl)methylene)bis(1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione) Diethylaminium Salt ***(4c)***

4c was prepared from 1,3-dimethylbarbutric acid **1a**, and *p*-nitrobenzaldehyde according to the general procedure (**GP1**) yielding a yellow powder (1.35 g, 2.61 mmol, 87%); m.p.: 195 °C; IR (KBr, cm^{-1}): 3453, 3205, 2987, 2904, 1675, 1608, 1576, 1511, 1438, 1343, 1254; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 17.58 (s, 1H, OH), 8.08 (d, 2H, J = 8.8 Hz, Ph), 7.29 (d, 2H, J = 8.8 Hz, Ph), 5.95 (s, 1H, benzyl-H), 3.34 (s, 12H, $4CH_3$), 3.07 (q, 4H, J = 7.3 Hz, CH_2CH_3), 1.29 (t, 6H, J = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.2, 164.4, 151.6, 150.8, 146.1, 127.5, 123.5, 91.4, 42.2, 34.9, 28.9, 28.7, 11.5; LC/MS (ESI): 518$[M]^+$; Anal. for $C_{23}H_{30}N_6O_8$; Calcd: C, 53.28; H, 5.83; N, 16.21; Found: C, 53.29; H, 5.85; N, 16.23.

The structure of **4c** was confirmed by X-ray crystal structure analysis (Bruker SMART APEXII CCD diffractometer). CCDC-1001798 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. A

colorless crystal suitable for X-ray analysis was obtained from recrystallization the compound from DCM/Et_2O at room temperature after 2 days.

5,5'-((4-Methoxyphenyl)methylene)bis(1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione) Diethylaminium Salt ***(4d)***

4d was prepared from 1,3-dimethylbarbutric acid **1a**, and *p*-methoxybenzaldehyde according to the general procedure (**GP1**) yielding rose-colored crystalline materials (1.35 g, 2.7 mmol, 90%). m.p.: 160 °C; IR (KBr, cm^{-1}): 3445, 3195, 2977, 2836, 1689, 1664, 1613, 1504, 1447, 1378, 1242; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 17.67 (s, 1H, OH), 7.01 (d, 2H, J = 8.8 Hz, Ph), 6.75 (d, 2H, J = 8.8 Hz, Ph), 5.79 (s, 1H, benzyl-H), 3.33 (s, 12H, $4CH_3$), 2.99 (q, 4H, J = 7.3 Hz, CH_2CH_3), 1.26 (t, 6H, J = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.3, 164.3, 157.4, 151.7, 133.6, 132.0, 127.4, 114.3, 92.1, 55.6, 42.1, 33.8, 28.9, 11.5; LC/MS (ESI): 503$[M]^+$; Anal. for $C_{24}H_{33}N_5O_7$; Calcd: C, 57.25; H, 6.61; N, 13.91; Found: C, 57.26; H, 6.61; N, 13.90.

5,5'-((3-Bromophenyl)methylene)bis(1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione) Diethylaminium Salt ***(4e)***

4e was prepared from 1,3-dimethylbarbutric acid **1a**, and *m*-bromobenzaldehyde according to the general procedure (**GP1**) yielding colorless crystalline materials (1.5g, 2.76 mmol, 92%). m.p.: 169 °C; IR (KBr, cm^{-1}): 3450, 3120, 2982, 1694, 1667, 1615, 1577, 1445, 1250; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 17.63 (s, 1H, OH), 7.22 (d, 1H, J = 7.3 Hz, Ph), 7.19 (s, 1H, Ph), 7.07 (d, 1H, J = 7.3 Hz, Ph), 7.05 (d, 1H, J = 7.3 Hz, Ph), 5.84 (s, 1H, benzyl-H), 3.34 (s, 6H, $2CH_3$), 3.32 (s, 6H, $2CH_3$), 3.02 (q, 4H, J = 7.3 Hz, CH_2CH_3), 1.27 (t, 6H, J = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.2, 164.4, 151.7, 144.7, 129.7,129.6, 128.7, 125.3, 91.5, 42.1, 34.4, 28.9, 28.7, 11.5; LC/MS

(ESI): 552[M]$^{+}$; Anal. for $C_{23}H_{30}BrN_5O_6$; Calcd: C, 50.01; H, 5.47; Br, 14.46; N, 12.68; Found: C, 50.03; H, 5.48; Br, 14.47; N, 12.71.

The structure of **4e** was confirmed by X-ray crystal structure analysis (Bruker SMART APEXII CCD diffractometer). CCDC-1001799 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. A colorless crystal suitable for X-ray analysis was obtained from recrystallization the compound from DCM/Et_2O at room temperature after 2 days.

5,5'-((4-hydroxyphenyl)methylene)bis(6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione) Diethylaminium Salt ***(4f)***

4f was prepared from 1,3-dimethylbarbutric acid **1a**, and *p*-hydroxybenzaldehyde according to the general procedure (**GP1**) yielding a yellow powder (1.3 g, 2.64 mmol, 88%); m.p.: 180 °C; IR (KBr, cm^{-1}): 3458, 3200, 2980, 2904, 1677, 1620, 1572, 1511, 1438, 1343, 1254; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 17.62 (s, 1H, OH), 7.31 (d, 2H, J = 8.8 Hz, Ph), 6.99 (d, 2H, J = 8.8 Hz, Ph), 5.79 (s, 1H, benzyl-H), 3.33 (s, 12H, 4CH_3), 3.03 (q, 4H, J = 7.3 Hz, CH_2CH$_3$), 1.27 (t, 6H, J = 7.3 Hz, CH$_2$CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.3, 164.4, 151.7, 141.1, 131.2, 128.5, 119.3, 91.7, 42.1, 34.2, 28.9, 28.7, 11.5; LC/MS (ESI): 489.52 [M]$^{+}$; Anal. for $C_{23}H_{31}N_5O_7$; Calcd: C, 56.43; H, 6.38; N, 14.31; Found: C, 56.44; H, 6.36; N, 14.30.

5,5'-(p-Tolylmethylene)bis(1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione) Diethylaminium Salt ***(4g)***

4g was prepared from 1,3-dimethylbarbituric acid **1a**, and *p*-tolualdehyde according to the general procedure (**GP1**) yielding colorless needle materials (1.41 g, 2.91 mmol, 97%). m.p.: 152 °C; IR (KBr, cm^{-1}): 3455, 3210, 2984, 2820, 1560, 1449, 1359; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 17.64 (s, 1H, OH), 6.99–6.96 (m, 4H, Ph), 5.80 (s, 1H, benzyl-H), 3.32 (s, 12H, $4CH_3$), 3.03 (q, 4H, J = 7.3 Hz, CH_2CH_3), 2.25 (s, 3H, CH_3), 1.28 (t, 6H, J = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.3, 164.3, 151.8, 138.6, 134.8, 128.9, 126.3, 92.1, 42.0, 34.2, 28.9, 28.6, 21.0, 11.4; LC/MS (ESI): 487$[M]^+$; Anal. for $C_{24}H_{35}N_5O_6$; Calcd: C, 59.12; H, 6.82; N, 14.36; Found: C,59.13; H, 6.81; N, 14.35.

The structure of **4b** was confirmed by X-ray crystal structure analysis (Bruker AXS GmbH). CCDC-957025 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. A colorless crystal suitable for X-ray analysis was obtained from recrystallization the compound from DCM/Et_2O at room temperature after 2 days.

5,5'-(Naphthalen-2-ylmethylene)bis(1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione) Diethylaminium Salt ***(4h)***

4h was prepared from 1,3-dimethylbarbutric acid **1a**, and 2-naphthaldehyde **2i** according to the general procedure (**GP1**) yielding beige powder (1.47 g, 2.82 mmol, 94%). m.p.: 146 °C; IR (KBr, cm^{-1}): 3454, 3200, 2967, 1668, 1585, 1438, 1250; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 17.33 (s, 1H, OH), 8.10 (d, 2H, J = 8.8 Hz, naphthyl-H), 7.99 (d, 2H, J = 8.8 Hz, naphthyl-H), 7.92 (d, 2H, J = 8.8 Hz, naphthyl-H), 7.90 (d, 2H, J = 8.8 Hz, naphthyl-H), 7.84 (d, 2H, J = 8.8 Hz, naphthyl-H), 7.68–7.38 (m, 3H, naphthyl-H), 6.37 (s, 1H, benzyl-H), 3.39 (s, 12H, $4CH_3$), 3.01 (q, 4H, J = 7.3 Hz, CH_2CH_3), 1.30 (t, 6H, J

= 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.9, 151.7, 136.8, 135.3, 134.3, 131.5, 129.1, 128.5, 127.0, 125.2 124.9, 123.8, 93.2, 41.8, 33.2, 28.8, 11.4; LC/MS (ESI): 523 $[M]^+$; Anal. for $C_{27}H_{33}N_5O_6$; Calcd: C, 61.94; H, 6.35; N, 13.38; Found: C, 61.95; H, 6.34; N, 13.40.

5,5'-(p-Tolylmethylene)bis(6-hydroxypyrimidine-2,4(1H,3H)-dione) Diethylaminium Salt ***(4i)***

4i was prepared from barbituric acid **1b**, and *p*-tolualdehyde according to the general procedure (**GP1**) yielding white powder (1.22 g, 2.85 mmol, 95%); m.p.: 205 C; IR (KBr, cm^{-1}): 3459, 3120, 2978, 2811, 1689, 1612, 1325, 1252; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 17.18 (s, 1H, OH), 10.09 (bs, 4H, NH), 6.93 (m, 4H, Ph), 5.90 (s, 1H, benzyl-H), 2.79 (q, 4H, J = 7.3 Hz, CH_2CH_3), 2.20 (s, 3H, CH_3), 1.07 (t, 6H, J = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 164.8, 164.1, 151.3, 142.1, 133.5, 128.5, 127.1, 91.6, 42.6, 30.6, 21.1, 13.0; LC/MS (ESI): 431$[M]^+$; Anal. for $C_{20}H_{25}N_5O_6$; Calcd: C, 55.68; H, 5.84; N, 16.23; Found: C, 55.67; H, 5.83; N, 16.22.

5,5'-((4-Chlorophenyl)methylene)bis(6-hydroxypyrimidine-2,4(1H,3H)-dione) Diethylaminium Salt ***(4j)***

4i was prepared from barbituric acid **1b**, and *p*-chlorobenzaldehyde according to the general procedure (**GP1**) yielding a white powder (1.28 g, 2.85 mmol, 95%); m.p.: 221 °C; IR (KBr, cm^{-1}): 3435, 3185, 2978, 2830, 1677, 1548, 1448, 1345, 1250; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 17.17 (s, 1H, OH), 10.00 (bs, 4H, NH), 7.18 (m, 4H, Ph), 5.93 (s, 1H, benzyl-H), 2.88 (q, 4H, J = 7.3 Hz, CH_2CH_3), 1.12 (t, 6H, J = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 164.7, 164.0, 151.2, 144.6, 133.5, 129.9, 129.1,

127.8, 91.3, 42.1, 30.7, 11.8; LC/MS (ESI): 451[M]$^+$; Anal. for $C_{19}H_{22}ClN_5O_6$; Calcd C, 50.50; H, 4.91; Cl, 7.85; N, 15.50; Found: C, 50.51; H, 4.90; Cl, 7.83; N, 15.51.

5,5'-((4-Methoxyphenyl)methylene)bis(6-hydroxypyrimidine-2,4(1H,3H)-dione) Diethylaminium Salt ***(4K)***

4k was prepared from barbituric acid **1b**, and *p*-methoxybenzaldehyde according to the general procedure (**GP1**) yielding a beige powder (1.22 g, 2.73 mmol, 91%); m.p.: 195 °C; IR (KBr, cm^{-1}): 3449, 3190, 2991, 2835, 1688, 1592, 1505, 1383, 1247; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 17.26 (s, 1H, OH), 9.99 (bs, 4H, NH), 6.92 (d, 2H, J = 8.0 Hz, Ph), 6.72 (d, 2H, J = 8.0 Hz, Ph), 5.88 (s, 1H, benzyl-H), 2.90 (q, 4H, J = 7.3 Hz, CH_2CH$_3$), 1.14 (t, 6H, J = 7.3 Hz, CH$_2$CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 164.6, 164.0, 157.0, 151.2, 137.2, 132.4, 115.1, 91.7, 55.4, 42.1, 30.7, 11.6; LC/MS (ESI): 447[M]$^+$; Anal. for $C_{20}H_{25}N_5O_7$; Calcd C, 53.69; H, 5.63; N, 15.65; Found: C, 53.69; H, 5.63; N, 15.66.

5,5'-(Naphthalen-2-ylmethylene)bis(6-hydroxypyrimidine-2,4(1H,3H)-dione) Diethylaminium Salt ***(4l)***

4l was prepared from barbituric acid **1b**, and 2-naphthaldehyde according to the general procedure (**GP1**) yielding a beige powder (1.3 g, 2.79 mmol, 93%); m.p.: 192 °C; IR (KBr, cm^{-1}): 3459, 3208, 2994, 1677, 1579, 1448, 1386, 1354; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 16.92 (s, 1H, OH), 10.41 (bs, 4H, NH), 8.13 (d, 1H, J = 8.8 Hz, naphthyl), 7.81(d, 1H, J = 8.8Hz, naphthyl), 7.63 (d, 1H, J = 8.8 Hz, naphthyl), 7.38–7.32 (m, 4H, naphthyl), 6.46 (s, 1H, benzyl-H), 2.79 (q, 4H, J = 7.3 Hz, CH_2CH$_3$), 1.08 (t, 6H, J = 7.3 Hz, CH$_2$CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 164.9, 151.1,141.5, 135.8,

134.0,132.4, 129.3, 128.7, 126.0,125.8, 125.5, 125.2, 124.9, 123.8, 92.3, 42.5, 29.7, 12.7; LC/MS (ESI): 467[M]$^{+}$; Anal. for $C_{23}H_{25}N_5O_6$; Calcd C, 59.09; H, 5.39; N, 14.98; Found: C, 59.12; H, 5.40; N, 15.01.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(phenyl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate ***(4m)***

4m was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone **2** and benzaldehyde according to the general procedure (**GP1**) yielding colorless crystalline material (671 mg, 1.47 mmol, 98%). m.p: 159 °C; IR (KBr, cm^{-1}): 3150, 2959, 1667, 1617, 1585, 1422, 1256, 1227;^{1}H NMR (400 MHz, $CDCl_3$): δ 15.28 (s, 1H, OH), 7.17-7.04(m, 5H, Ph), 5.85 (s, 1H, benzyl-H), 3.29 (s, 12H, $4CH_3$), 2.96(q, 4H, J = 7.3Hz, CH_2CH_3), 2.42 (d, 2H, J = 5.1Hz, CH_2), 2.29 (m, 2H, CH_2), 1.24(t, 6H, J = 7.3Hz, CH_2CH_3), 1.14(s, 3H, CH_3), 1.05(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.5, 180.8, 152.5, 142.5, 128.0, 126.7, 125.1, 116.3, 90.9, 51.4, 45.9, 42.2, 33.0, 31.5, 29.6, 28.4, 27.6, 11.4; LC/MS (ESI): 457 [M]$^{+}$; Anal. for $C_{25}H_{35}N_3O_5$; calcd: C, 65.62; H, 7.71; N, 9.18;Found: C, 65.61; H, 7.73; N, 9.20.

The structure of **4m** was confirmed by X-ray crystal structure analysis. CCDC- 933624 contains the supplementary crystallographic data for this compound. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. A colorless crystal suitable for X-ray analysis was obtained from recrystallization of the compound from $CHCl_3/Et_2O$ at room temperature after 2 days.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(p-tolyl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4n)

4n was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone**2** and p-tolualdehyde according to the general procedure (**GP1**) yielding an oily material (685 mg, 1.45 mmol, 97%). IR (KBr, cm^{-1}): 3150, 2954, 2867, 1675, 1580, 1508, 1447, 1380, 1256, 1145;^{1}H NMR (400 MHz, $CDCl_3$): δ 15.25 (s, 1H, OH), 7.00-6.93(m, 4H, Ph), 5.84 (s, 1H, benzyl-H), 3.28 (s, 12H, $4CH_3$), 2.90(q, 4H, J = 7.3Hz, CH_2CH_3), 2.30 (d, 4H, J = 5.1Hz, CH_2), 2.22 (s, 3H, CH_3), 1.20(t, 6H, J = 7.3Hz, CH_2CH_3), 1.16(s, 3H, CH_3), 1.04(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 180.1, 152.8, 140.5, 134.2, 129.8, 128.7, 126.8, 126.7, 115.6, 91.0, 51.4, 45.9, 42.5, 32.6, 31.5, 29.6, 28.4, 27.6, 20.9, 11.9; LC/MS (ESI): 471 $[M]^+$; Anal. for $C_{26}H_{37}N_3O_5$; calcd: C, 66.22; H, 7.91; N, 8.91;Found: C, 66.24; H, 7.92; N, 8.87.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(4-methoxyphenyl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4o)

4o was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone**2** and anisaldehyde**3** according to the general procedure (**GP1**) yielding an oily material (672 mg, 1.38 mmol, 92%). IR (KBr, cm^{-1}): 3047, 2953, 2866, 2499, 1679, 1577, 1510, 1427, 1373, 1255, 1214;^{1}H NMR (400 MHz, $CDCl_3$): δ 15.26 (s, 1H, OH), 6.98(d, 2H, J = 8.0Hz, Ph), 6.72(d, 2H, J = 8.0Hz, Ph), 5.69 (s, 1H, benzyl-H), 3.71 (s, 3H, CH_3), 3.29 (s, 12H, $4CH_3$), 2.87(q, 4H, J = 7.3Hz, CH_2CH_3), 2.31 (d, 4H, J = 5.1Hz, CH_2), 1.19(t, 6H, J = 7.3Hz, CH_2CH_3), 1.12(s, 3H, CH_3), 1.03(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.1, 187.2, 157.1, 134.5, 133.9, 127.8, 127.6, 115.6, 113.4, 55.2, 42.6, 31.5, 31.1, 27.9,

12.2; LC/MS (ESI): 487 $[M]^+$; Anal. for $C_{26}H_{37}N_3O_6$; calcd: C, 64.05; H, 7.65; N, 8.62;Found: C, 64.11; H, 7.64; N, 8.59.

5-((4-Chlorophenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4p)

4p was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone**2** and *p*-chlorobenzaldehyde**3** according to the general procedure (**GP1**) yielding an oily material (715 mg, 1.45 mmol, 97%). IR (KBr, cm^{-1}): 3151, 2955, 2868, 2497, 1675, 1580, 1481, 1444, 1379, 1258, 1206;^{1}H NMR (400 MHz, $CDCl_3$): δ 15.02 (s, 1H, OH), 7.12-6.95(m, 4H, Ph), 5.87 (s, 1H, benzyl-H), 3.30 (s, 12H, $4CH_3$), 2.90(q, 4H, J = 7.3Hz, CH_2CH_3), 2.38 (s, 4H, CH_2), 1.20(t, 6H, J = 7.3Hz, CH_2CH_3), 1.16(s, 3H, CH_3), 1.04(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.1, 181.0, 152.5, 141.5, 130.6, 128.3, 128.2, 128.0, 127.9, 115.2, 90.7, 65.9, 49.8, 42.3, 32.4, 31.5, 31.2, 29.6, 28.4, 27.6, 15.3, 11.4; LC/MS (ESI): 492 $[M]^+$; Anal. for $C_{25}H_{34Cl}N_3O_5$; calcd: C, 61.03; H, 6.97; Cl, 7.21; N, 8.54;Found: C, 61.06; H, 7.00; Cl, 7.18; N, 8.57.

5-((4-Bromophenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4q)

4q was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone**2** and *p*-bromobenzaldehyde**3** according to the general procedure (**GP1**) yielding an oily material (761 mg, 1.42 mmol, 95%). IR (KBr, cm^{-1}): 3155, 2955, 2867, 2500, 1674, 1579, 1430, 1376, 1204;^{1}H NMR (400 MHz, $CDCl_3$): δ 15.20 (s, 1H, OH), 7.34(d, 2H, J = 8.0Hz, Ph), 6.98(d, 2H, J = 8.0Hz, Ph), 5.79 (s, 1H, benzyl-H), 3.27 (s, 12H, $4CH_3$), 2.99(q, 4H, J = 7.3Hz, CH_2CH_3), 2.40 (d, 2H, J = 5.1Hz, CH_2), 2.28(m, 2H, CH_2), 1.29(t, 6H, J =

7.3Hz, CH_2CH_3), 1.18(s, 3H, CH_3), 1.04(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.1, 191.2, 164.8, 152.4, 142.8, 132.5, 131.0, 129.9, 128.7, 128.6, 118.9, 115.9, 90.6, 51.2, 45.8, 42.3, 32.7, 31.5, 29.5, 28.5, 28.3, 27.6, 11.4; LC/MS (ESI): 536 $[M]^+$; Anal. for $C_{25}H_{34}BrN_3O_5$; calcd: C, 55.97; H, 6.39; Br, 14.89; N, 7.83;Found: C, 56.00; H, 6.40; Br, 14.86; N, 7.82.

5-((3-Bromophenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4r)

4r was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone **2** and *m*-bromobenzaldehyde **3** according to the general procedure (**GP1**) yielding an oily material (745 mg, 1.39 mmol, 93%). IR (KBr, cm^{-1}): 3050, 2955, 2868, 2500, 1675, 1581, 1444, 1378, 1255, 1205; ^{1}H NMR (400 MHz, $CDCl_3$): δ 15.63 (s, 1H, OH), 7.22 (d, 1H, J = 7.3Hz, Ph), 7.19 (s, 1H, Ph), 7.07 (d, 1H, J = 7.3Hz, Ph), 7.05 (d, 1H, J = 7.3Hz, Ph), 5.84 (s, 1H, benzyl-H), 3.34(s, 6H, $2CH_3$), 3.32(s, 6H, $2CH_3$), 2.98(q, 4H, J = 7.3Hz, CH_2CH_3), 2.31 (d, 4H, J = 5.1Hz, CH_2), 1.24(t, 6H, J = 7.3Hz, CH_2CH_3), 1.12(s, 3H, CH_3), 1.03(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.8, 186.4, 165.2, 164.4, 151.7, 144.7, 129.7,129.6, 128.7, 125.3, 91.5, 42.1, 34.4, 28.9, 28.7, 11.5; LC/MS (ESI): 536 $[M]^+$; Anal. for $C_{25}H_{34}BrN_3O_5$; calcd: C, 55.97; H, 6.39; Br, 14.89; N, 7.83;Found: C, 56.01; H, 6.41; Br, 14.86; N, 7.84.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(1-nitrophenyl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4s)

4s was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone **2** and *o*-nitrobenzaldehyde**3** according to the general procedure (**GP1**) yielding a beige material (690 mg, 1.37 mmol, 92%). m.p: 146 °C; IR (KBr, cm^{-1}): 3054, 2953, 2865, 2500, 1673,

1580, 1510, 1427, 1373, 1255, 1214;^{1}H NMR (400 MHz, $CDCl_3$): δ 15.33 (s, 1H, OH), 7.01-7.35 (m, 3H, Ph), 5.65 (s, 1H, benzyl-H), 3.70 (s, 12H, $4CH_3$), 2.89(q, 4H, J = 7.3Hz, CH_2CH_3), 2.30(d, 4H, J = 14.7Hz, CH_2), 1.15(t, 6H, J = 7.3Hz, CH_2CH_3), 1.10(s, 3H, CH_3), 1.00(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.6, 153.2, 145.5, 141.6, 129.1, 128.2, 127.8, 125.8, 88.5, 49.1, 41.9, 27.5, 11.5; LC/MS (ESI): 502$[M]^+$; Anal. for $C_{25}H_{34}N_4O_7$; calcd: C, 59.75; H, 6.82; N, 11.15; Found: C, 59.72; H, 6.80; N, 11.17.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(4-(dimethylamino)phenyl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4t)

4t was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone **2** and *p-(dimethylamino)*benzaldehyde**3** according to the general procedure (**GP1**) yielding a beige material (550 mg, 1.1 mmol, 73%). m.p: 165 °C; IR (KBr, cm^{-1}): 3055, 2950, 2865, 2500, 1669, 1580, 1510, 1427, 1373, 1255, 1214;^{1}H NMR (400 MHz, $CDCl_3$): δ 15.33 (s, 1H, OH), 7.02 (d, 2H, J = 8.0Hz, Ph), 6.75 (d, 2H, J = 8.8Hz, Ph), 5.69 (s, 1H, benzyl-H), 3.70 (s, 12H, $4CH_3$), 3.01 (s, 6H, $N(CH_3)_2$), 2.89(q, 4H, J = 7.3Hz, CH_2CH_3), 2.31(d,4H, J = 14.7Hz, CH_2), 1.15(t, 6H, J = 7.3Hz, CH_2CH_3), 1.12(s, 3H, CH_3), 1.00(s, 3H, CH_3) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.6, 153.2, 145.5, 141.6, 129.1, 128.2, 127.8, 125.8, 88.5, 49.1, 41.9, 41.8, 27.5, 11.5; LC/MS (ESI): 499.29 $[M]^+$; Anal. for $C_{27}H_{39}N_4O_5$; calcd: C, 64.91; H, 7.87; N, 11.21 ;Found: C, 64.90; H, 7.87; N, 11.23.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(4-hydroxyphenyl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4v)

4v was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone**2** and *p*-hydroxybenzaldehyde**3** according to the general procedure (**GP1**) yielding a white solid

material (645 mg, 1.36 mmol, 91%). m.p: 162 °C; IR (KBr, cm^{-1}): 23097, 2939, 2884, 2828, 2498, 1747, 1574, 1530, 1506, 1466, 1384, 1241;^{1}H NMR (400 MHz, DMSO-d_6): δ 14.52 (s, 1H, OH), 8.50 (brs, 1H, OH), 6.76(d, 2H, J = 8.0Hz, Ph), 6.50(d, 2H, J = 8.0Hz, Ph), 6.04(s, 1H, benzyl-H), 3.07 (s, 12H, $2CH_3$), 3.14(q, 4H, J = 7.3Hz, CH_2CH_3), 2.92 (q, 4H, J = 13.9Hz, CH_2), 206 (s, 4H, CH_2), 1.12(t, 6H, J = 7.3Hz, CH_2CH_3), 0.98(s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 198.0, 188.5, 154.1, 136.6, 128.3, 115.3, 114.3, 90.1, 50.9, 45.5, 42.1, 31.6, 30.7, 29.7, 11.7; LC/MS (ESI): 473 $[M]^+$; Anal. for $C_{25}H_{35}N_3O_6$; calcd: C, 63.41; H, 7.45; N, 8.87;Found: C, 63.40; H, 7.43; N, 8.85.

4-((6-hydroxy-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)benzaldehyde Diethylaminium Salt ***(4x)***

Pure product **4x** was obtained according to **GP1** as solid (1.26 g, 90%). IR (cm^{-1}): 3156, 2950, 2872, 1678, 1590, 1508, 1375, 1256, 1232, 1167; ^{1}H-NMR ($CDCl_3$, 400 MHz): 14.16 (s, 1H, OH), 9.80 (s, 1H, CHO), 8.01 (brs, 2H, NH), 6.98 (d, 2H, J = 7.3 Hz, Ph), 6.75 (d, 2H, J = 7.3 Hz, Ph), 5.61 (s, 1H, benzyl-H), 3.73 (s, 6H, CH_3), 2.92 (q, 4H, J = 7.3 Hz, CH_2CH_3), 2.31 (m, 4H, $2CH_2$), 1.26(t, 6H, J = 7.3Hz, CH_2CH_3), 1.05(s, 3H, CH_3), 1.00(s, 3H, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 193.0, 188.1, 165.0, 157.2, 127.8, 115.7,113.8, 91.6, 55.2, 48.8, 48.6, 42.4, 31.5, 29.4, 27.7, 11.7; LC/MS (ESI): 485.57 $[M]^+$; Anal. for $C_{26}H_{35}N_3O_6$; Calcd: C, 64.31; H, 7.27; N, 8.65; Found: C, 64.30; H, 7.26; N, 8.63.

5-((2,4-Dichlorophenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate ***(4w)***

4w was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone **2** and 2,4-dichlorobenzaldehyde according to the general procedure (**GP1**) yielding a beige solid material (710 mg, 1.35 mmol, 90%). m.p: 164 °C; IR (KBr, cm^{-1}): 3059, 2995, 2867, 2114, 1741, 1658, 1591, 1463, 1429, 1370, 1341, 1256, 1201^{1}H-NMR (400 MHz, $CDCl_3$): δ 14.80 (s, 1H, OH), 7.29 (d, 1H, J = 8.0Hz, Ph), 7.19 (s, 1H, Ph), 7.12(d, 2H, J = 8.0Hz, Ph), 5.76 (s, 1H, benzyl-H), 3.28 (s, 12H, $4CH_3$), 3.07(q, 4H, J = 7.3Hz, CH_2CH_3), 2.37 (s, 2H, CH_2), 2.27 (d, 2H, J = 5.1Hz, CH_2), 1.34(t, 6H, J = 7.3Hz, CH_2CH_3), 1.04(s, 3H, CH_3), 1.01(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.1, 165.4, 164.4, 152.5, 139.8, 133.6, 131.7, 131.2, 129.3, 126.4, 115.7, 89.8, 51.2, 45.7, 41.9, 32.4, 31.2, 28.3, 28.2, 11.3; LC/MS (ESI): 526 $[M]^+$; Anal. for $C_{25}H_{33}Cl_2N_3O_5$; calcd: C, 57.04; H, 6.32; Cl, 13.47; N, 7.98;Found: C, 57.09; H, 6.31; Cl, 13.44; N, 8.01.

5-((2,6-Dichlorophenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4y)

4y was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone **2** and 2,6-dichlorobenzaldehyde **3** according to the general procedure (**GP1**) yielding an oily material (702 mg, 1.33 mmol, 89%). IR (KBr, cm^{-1}): 3048, 2955, 2869, 2728, 2494, 1676, 1575, 1428, 1372, 1238, 1196;^{1}H NMR (400 MHz, $CDCl_3$): δ 14.80 (s, 1H, OH), 7.36 (d, 2H, J = 8.0Hz, Ph), 7.29 (t, 1H, J = 8.0Hz, Ph), 7.12(d, 2H, J = 8.0Hz, Ph), 5.98 (s, 1H, benzyl-H), 3.26 (s, 12H, $4CH_3$), 2.92(q, 4H, J = 7.3Hz, CH_2CH_3), 2.37 (s, 2H, CH_2), 2.27 (d, 2H, J = 5.1Hz, CH_2), 1.24(t, 6H, J = 7.3Hz, CH_2CH_3), 1.094(s, 3H, CH_3), 1.04(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.8, 188.9, 165.3, 164.3, 152.5,

149.7, 137.4, 131.5, 129.8, 126.5, 124.2, 115.5, 114.7, 89.9, 53.5, 41.4, 31.9, 28.7, 28.2, 11.4 ; LC/MS (ESI): 526 $[M]^+$; Anal. for $C_{25}H_{33}Cl_2N_3O_5$; calcd: C, 57.04; H, 6.32; Cl, 13.47; N, 7.98; Found: C, 57.08; H, 6.30; Cl, 13.45; N, 8.00.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(naphthalen-2-yl)methyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (4z)

4z was prepared from 1,3-dimethylbarbituric acid **1a**, dimedone **2** and 2-naphthaldehyde **3** according to the general procedure (**GP1**) yielding a white solid material (715 mg, 1.41 mmol, 94%). m.p: 170 °C; IR (KBr, cm^{-1}): 2994, 2948, 2866, 2506, 1742, 1651, 1603, 1570, 1526, 1473, 1431, 1362, 1245;^{1}H NMR (400 MHz, $CDCl_3$): δ 14.26 (s, 1H, OH), 7.46-7.22(m, 7H, naphthyl), 6.20 (s, 1H, benzyl-H), 3.26 (s, 6H, $2CH_3$), 3.23 (s, 6H, $2CH_3$), 3.14(q, 4H, J = 7.3Hz, CH_2CH_3), 2.41 (q, 4H, J = 5.1Hz, CH_2), 2.23 (s, 2H, CH_2), 1.37(t, 6H, J = 7.3Hz, CH_2CH_3), 1.07(s, 3H, CH_3), 1.01(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.0, 180.5, 165.3, 164.3, 152.5, 149.7, 136.8, 131.5, 129.9, 126.5, 124.2, 115.5, 114.7, 89.9, 50.9, 45.5, 41.7, 31.3, 30.7, 28.2, 11.1; LC/MS (ESI): 507 $[M]^+$; Anal. for $C_{29}H_{37}N_3O_5$; calcd: C, 68.62; H, 7.35; N, 8.28; Found: C, 68.65; H, 7.34; N, 8.30.

Diethylammonium-2-((2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(phenyl)methyl)-5,5-dimethyl-3-oxocyclohex-1-enolate ***5a***

Pure product **5a** was obtained according to **GP1** as solid (1.26 g, 95%). IR (cm^{-1}): 2955 (s), 1586 (s), 1382 (s), 776 (s), 576 (s), 480 (s); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.95 – 1.14 (m, 12H, C**H**$_3$), 1.18 (t, J = 6.60 Hz, 6H, $NHCH_2C\mathbf{H}_3$), 2.31 (s, 8H, C**H**$_2$+ COC**H**$_2$), 2.84 (q,J = 6.60 Hz, 4H, $NHC\mathbf{H}_2CH_3$), 5.74 (s, 1H, PhC**H**), 7.01 – 7.21 (m,

5H. Ar**H**), 8.25 (bs,1H. N**H**$_2$), 13.91 (s, O**H**); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 11.4 (**C**H_3CH_2NH), 31.5 (**C**$H_3)_2$, 32.0 {**C**$(CH_3)_2$}, 34.2 (Ph-**C**), 42.3 (CH_3**C**H_2NH), 45.9, 50.6, 115.5, 125.2 (Ph**C4**), 126.8 (Ph**C2**), 128.0 (Ph**C3**), 142.4 (Ph**C1**), 179.3 (**C**-OH), 199.1 (**C**=O);Anal. Calcd. for $C_{27}H_{37}NO_4$: C, 73.36; H, 8.98; N, 3.07; O, 14.57; Found: C, 73.43; H, 8.90; N, 3.17; O, 14.49;: LC/MS (ESI): *m/z* = 441.29 $[M]^+$.

*Diethylammonium 2-((2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(p-tolyl)methyl)-5,5-dimethyl-3-oxocyclohex-1-enolate **5b***

Pure product **5b** was obtained according to **GP1** as solid (1.2 g, 93%). IR (cm^{-1}): 2957 (s), 1571 (s), 1483 (s), 1383 (s), 1267 (s), 739 (s), 488 (s); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.94 – 1.16 (m, 12H, C**H**$_3$), 1.18 (t, *J* = 7.32 Hz, 6H, NH_2CH_2C**H**$_3$), 2.23 (s, 3H, PhC**H**$_3$), 2.31 (s, 8H, C**H**$_2$+ COC**H**$_2$), 2.84 (q, *J* = 7.32 Hz, 4H, NHC**H**$_2CH_3$), 5.73 (s, 1H, PhC**H**), 6.91 – 7.05 (m, 4H. Ar**H**), 7.83 (bs,2H. N**H**$_2$), 13.73 (s, O**H**); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 12.4 (**C**H_3CH_2NH), 20.9 (Ph**C**H_3), 31.4 (**C**$H_3)_2$, 32.7 {**C**$(CH_3)_2$}, 34.9 (Ph-**C**), 42.7 (CH_3**C**H_2NH), 46.1, 51.8, 115.6, 126.8 (Ph**C4**), 128.6 (Ph**C2**), 134.0 (Ph**C3**), 144.4 (Ph**C1**), 187.3 (**C**-OH), 195.8 (**C**=O);Anal. Calcd. for$C_{28}H_{41}NO_4$: C, 73.79; H, 9.14; N, 3.09; O, 13.91; Found: C, 73.81; H, 9.07; N, 3.07; O, 14.05: LC/MS (ESI): *m/z* = 455.30 $[M]^+$.

*Diethylammonium 2-((2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(m-tolyl)methyl)-5,5-dimethyl-3-oxocyclohex-1-enolate **5c***

Pure product **5c** was obtained according to **GP1** as solid (1.24 g,91%). IR (cm^{-1}): 2952 (s), 1572 (s), 1483 (s), 1381 (s), 1227 (s), 1143 (s), 787 (s), 463 (s); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.91 – 1.12 (m, 12H, C**H**$_3$), 1.16 (t, *J* = 7.36 Hz, 6H, NH_2CH_2C**H**$_3$), 2.28 (s, 3H, PhC**H**$_3$), 2.38 (s, 8H, C**H**$_2$+ COC**H**$_2$), 2.91 (q, *J* = 7.36 Hz, 4H, NHC**H**$_2CH_3$

), 5.71 (s, 1H, PhC**H**), 6.88 – 7.03 (m, 4H. Ar**H**), 7.85 (bs,2H. N**H**$_2$), 13.78 (s, O**H**); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 12.3 (**C**H_3CH_2NH), 20.6 (Ph**C**H_3), 31.2 (**C**$H_3)_2$, 32.8 {**C**$(CH_3)_2$}, 34.8 (Ph-**C**), 42.6 (CH_3**C**H_2NH), 46.3, 51.9, 115.8, 126.9 (Ph**C4**), 128.4 (Ph**C2**), 134.1 (Ph**C3**), 144.7 (Ph**C1**), 187.5 (**C**-OH), 195.9 (**C**=O); Anal. Calcd. for $C_{28}H_{41}NO_4$: C, 73.85; H, 9.09; N, 3.13; O, 13.79; Found: C, 73.81; H, 9.07; N, 3.07; O, 14.05: LC/MS (ESI): *m/z* = 455.30 $[M]^+$.

Diethylammonium 2-((2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(4-methoxyphenyl)methyl)-5,5-dimethyl-3-oxocyclohex-1-enolate ***5d***

Pure product **5d** was obtained according to **GP1** as solid (1.26 g, 89%). IR (cm^{-1}): 3121 (s), 1668 (s), 1614 (s), 1578 (s), 1446 (s), 778 (s), 608 (s), 457 (s); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.96 – 1.16 (m, 12H, C**H**$_3$), 1.20 (t, *J* = 7.36 Hz, 6H, NH_2CH_2C**H**$_3$),2.30 (s, 8H, C**H**$_2$+ COC**H**$_2$), 2.85 (q, *J* = 7.36 Hz, 4H, NHC**H**$_2CH_3$), 3.72 (s, 3H, OC**H**$_3$), 5.72 (s, 1H, PhC**H**), 6.72 (d,*J* = 7.40 Hz, 2H, Ar**H**),6.97 (d, *J* = 7.40 Hz, 2H. Ar**H**),8.22 (bs,2H. N**H**$_2$), 14.67 (s, O**H**); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ11.9 (**C**H_3CH_2NH), 31.1 {**C**$(CH_3)_2$}, 31.5(**C**$H_3)_2$, 34.1 (Ph-**C**), 42.5 (CH_3**C**H_2NH), 45.3, 50.7, 55.2 (PhO**C**H_3), 113.4, 115.7 (Ph**C3**), 127.8 (Ph**C2**), 133.1 (Ph**C1**), 157.6 (Ph**C4**), 187.5 (**C**-OH), 194.1 (**C**=O); Anal. Calcd. for $C_{28}H_{41}NO_5$: C, 71.19; H, 8.79; N, 3.05; O, 17.11; Found: C, 71.31; H, 8.76; N, 2.97; O, 16.96: LC/MS (ESI): *m/z* = 471.30 $[M]^+$.

Diethylammonium 2-((2,6-dichlorophenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-5,5-dimethyl-3-oxocyclohex-1-enolate ***5e***

Pure product **5e** was obtained according to **GP1** as solid (1.39 g, 91%). IR (cm^{-1}): 2953 (s), 2869 (s), 1711 (s), 1575 (s), 1497 (s), 1367 (s), 1220 (s), 776 (s), 448 (s); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.88 – 1.03 (bs, 12H, C**H**$_3$), 1.17 (t, *J* = 7.36 Hz, 6H,

$NH_2CH_2C\mathbf{H}_3$), 2.19 (bs, 8H, C$\mathbf{H}_2$+ COC$\mathbf{H}_2$), 2.90 (q, *J* = 7.36 Hz, 4H, NHC$\mathbf{H}_2CH_3$), 5.89 (s, 1H, PhC**H**), 6.95 (d, *J* = 14.4 Hz, 1H, Ar**H**), 7.16 (m, 1H, Ar**H**), 7.24(s, *J* = 14.4 Hz, 1H, Ar**H**), 8.71 (bs,2H. N$\mathbf{H}_2$), 14.78 (s, O**H**); ^{13}C-NMR (DMSO-d_6,100 MHz): δ 11.9 (**C**H_3CH_2NH), 30.3 {**C**$(CH_3)_2$}, 31.8 (**C**$H_3)_2$, 34.3 (Ph-**C**), 42.5 (CH_3**C**H_2NH), 47.6, 51.1, 114.2, 125.9 (Ph**C3**), 128.2 (Ph**C4**), 134.9 (Ph**C2**), 139.1 (Ph**C1**), 189.1 (**C**-OH), 198.3 (**C**=O); Anal. Calcd. for $C_{27}H_{37}Cl_2NO_4$: C, 63.46; H, 7.55; N, 2.43; O, 12.91; Found: C, 63.52; H, 7.31; N, 2.74; O, 12.54; LC/MS (ESI): *m/z* = 509.21 $[M]^+$.

Diethylammonium 2-((2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(3-nitrophenyl)methyl)-5,5-dimethyl-3-oxocyclohex-1-enolate ***5f***

Pure product **5f** was obtained according to **GP1** as solid (1.26 g, 90%). IR (cm^{-1}): 2872 (s), 1582 (s), 1510 (s), 1466 (s), 1384 (s), 1339 (s), 757 (s), 487 (s); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.91 – 1.06 (m, 12H, C$\mathbf{H}_3$), 1.21 (t, *J* = 7.32 Hz, 6H, $NH_2CH_2C\mathbf{H}_3$),2.29 (s, 8H, C$\mathbf{H}_2$+ COC$\mathbf{H}_2$), 2.94 (q, *J* = 7.32 Hz, 4H, NHC$\mathbf{H}_2CH_3$), 5.92 (s, 1H, PhC**H**), 7.21 (d, *J* = 8.80 Hz, 2H, Ar**H**), 8.01 (m, *J* = 8.80 Hz, 2H.Ar**H**),8.32(bs,2H. N$\mathbf{H}_2$), 15.12 (s, O**H**); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 11.4 (**C**H_3CH_2NH), 31.6{**C**$(CH_3)_2$}, 32.2 (**C**$H_3)_2$, 34.1 (Ph-**C**), 42.5 (CH_3**C**H_2NH), 45.2, 50.3, 114.8, 123.2 (Ph**C3**), 127.7 (Ph**C2**), 145.5 (Ph**C4**), 151.9 (Ph**C1**), 186.8 (**C**-OH), 194.9 (**C**=O); Anal. Calcd. for$C_{27}H_{38}N_2O_6$: C, 66.74; H, 7.98; N, 5.55; O, 19.91; Found: C, 66.64; H, 7.87; N, 5.76; O, 19.73: LC/MS (ESI): *m/z* = 468.27 $[M]^+$.

Diethylammonium 2-((4-formylphenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-5,5-dimethyl-3-oxocyclohex-1-enolate ***5g***

Pure product **5g** was obtained according to **GP1** as solid (1.01 g, 75%). IR (cm^{-1}): 3150 (s), 1586 (s), 1519 (s), 1469 (s), 1381 (s), 1339 (s), 779 (s), 495 (s); ^{1}H-NMR

(DMSO-d_6, 400 MHz) δ 0.88 – 1.01 (m, 12H, C**H**$_3$), 1.15 (t, J = 7.32 Hz, 6H, NH_2CH_2C**H**$_3$), 2.10 (s, 8H, C**H**$_2$+ COC**H**$_2$), 2.89 (q, J = 7.32 Hz, 4H, NHC**H**$_2CH_3$), 3.00 (s, 6H, N$(CH_3)_2$), 6.08 (s, 1H, PhC**H**), 6.49 (d, J = 8.04 Hz, 2H, Ar**H**), 6.78 (m, J = 8.04 Hz, 2H. Ar**H**), 8.39 (bs, 2H. N**H**$_2$), 16.45 (s, O**H**); ^{13}C-NMR (DMSO-d_6,100 MHz): δ 11.8 (**C**H_3CH_2NH), 29.8 {**C**$(CH_3)_2$}, 31.9 (**C**$H_3)_2$, 34.2 (Ph-**C**), 41.7 (CH_3)**)**$_2$NH), 42.0 (CH_3**C**H_2NH), 45.6, 50.9, 114.3, 115.3 (Ph**C3**), 128.3 (Ph**C2**), 136.1 (Ph**C1**), 154.1 (Ph**C4**), 183.6 (**C**-OH), 196.1 (**C**=O); Anal. Calcd. for $C_{28}H_{39}NO_5$: C, 71.61; H, 8.37; N, 2.98; Found: C, 71.61; H, 8.37; N, 2.98; LC/MS (ESI): *m/z* = 69.28 $[M]^+$.

Diethylammonium 2-((2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(4-hydroxyphenyl)methyl)-5,5-dimethyl-3-oxocyclohex-1-enolate ***5h***

Pure product **5h** was obtained according to **GP1** as solid (1.01 g, 88%). IR (cm^{-1}): 3157 (s), 1584 (s), 1519 (s), 1469 (s), 1381 (s), 1339 (s), 779 (s), 495 (s); ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 0.85 – 0.97 (m, 12H, C**H**$_3$), 1.12 (t, J = 7.32 Hz, 6H, NH_2CH_2C**H**$_3$), 2.06 (s, 8H, C**H**$_2$+ COC**H**$_2$), 2.50 (s, 1H, PhO**H**), 2.88 (q, J = 7.32 Hz, 4H, NHC**H**$_2CH_3$), 6.04 (s, 1H, PhC**H**), 6.45 (d, J = 8.04 Hz, 2H, Ar**H**), 6.75 (m, J = 8.04 Hz, 2H. Ar**H**), 8.32 (bs, 2H. N**H**$_2$), 16.41 (s, O**H**); ^{13}C-NMR (DMSO-d_6,100 MHz): δ 11.8 (**C**H_3CH_2NH), 29.8 {**C**$(CH_3)_2$}, 31.9 (**C**$H_3)_2$, 34.2 (Ph-**C**), 42.0 (CH_3**C**H_2NH), 45.6, 50.9, 114.3, 115.3 (Ph**C3**), 128.3 (Ph**C2**), 136.1 (Ph**C1**), 154.1 (Ph**C4**), 183.6 (**C**-OH), 196.1 (**C**=O); Anal. Calcd. for $C_{27}H_{39}NO_5$: C, 70.74; H, 8.89; N, 3.13; O, 17.61; Found: C, 70.87; H, 8.59; N, 3.06; O, 17.48; LC/MS (ESI): *m/z* = 383.19 $[M]^+$.

4-((6-Hydroxy-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)(6-hydroxy-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzaldehyde Diethylaminium Salt ***(5i)***

Pure product **5i** was obtained according to **GP1** as white solid (1.20 g, 88%). IR (cm^{-1}): 3455, 3305, 3000, 2910, 1677, 1582, 1510, 1466, 1384, 1339; ^{1}H-NMR ($CDCl_3$, 400 MHz) 17.30 (s, 1H, OH), 9.90 (s, 1H, CHO), 8.23 (brs, 2H, NH), 7.56 (d, 2H, *J* = 8.0 Hz, Ph), 7.11 (d, 2H, *J* = 8.0 Hz, Ph), 5.85 (s, 1H, benzyl-H), 3.34 (s, 12H, $4CH_3$), 3.03 (q, 4H, *J* = 7.3 Hz, CH_2CH_3), 1.25 (t, 6H, *J* = 7.3 Hz, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 192.1, 165.2, 164.1, 151.2, 150.0, 134.1, 129.5, 127.5, 91.6, 42.2, 35.1, 29.0, 28.7, 11.5; LC/MS (ESI): 473.48 $[M]^+$; Anal. for $C_{22}H_{27}N_5O_7$; Calcd: C, 55.81; H, 5.75; N, 14.79; Found: C, 55.83; H, 5.76; N, 14.81.

5-((4-Chlorophenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (5j)

5j was prepared from barbituric acid **1b**, dimedone **2** and *p*-chlorobenzaldehyde **3** according to the general procedure (**GP1**) yielding an oily product (625 mg, 1.35 mmol, 90%). IR (KBr, cm^{-1}): 3049, 2954, 2865, 2499, 1738, 1699, 1590, 1483, 1375, 1292, 1258, 1225, 1205;^{1}H NMR (400 MHz, $CDCl_3$ δ 13.32 (s, 1H, OH), 8.83 (brs, 2H, NH), 7.27(d, 2H, *J* = 8.0Hz, Ph), 7.00(d, 2H, *J* = 8.0Hz, Ph), 5.89 (s, 1H, benzyl-H), 2.88(q, 4H, *J* = 7.3Hz, CH_2CH_3), 2.31 (d, 4H, *J* = 5.1Hz, CH_2), 1.19(t, 6H, *J* = 7.3Hz, CH_2CH_3), 1.09(s, 3H, CH_3), 1.03(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.9, 141.0, 134.8, 131.0, 129.5, 128.3, 115.3, 91.1, 47.1, 42.7, 31.6, 31.5, 29.1, 28.2, 27.8, 11.3; LC/MS (ESI): 463 $[M]^+$; Anal. for $C_{23}H_{30}ClN_3O_5$; calcd: C, 59.54; H, 6.52; Cl, 7.64; N, 9.06;Found: C, 59.57; H, 6.51; Cl, 7.60; N, 9.02.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(phenyl)methyl)-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (5k)

5k was prepared from barbituric acid **1b**, dimedone **2** and benzaldehyde **3** according to the general procedure (**GP1**) yielding a white solid material (598 mg, 1.39 mmol, 93%). m.p: 215 °C; IR (KBr, cm^{-1}): 3027, 2948, 2867, 2156, 1683, 1593, 1451, 1374, 1291, 1257, 1141^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.26 (s, 1H, OH), 9.31(brs, 2H, NH), 7.12(m, 5H, Ph), 5.52 (s, 1H, benzyl-H), 2.99(q, 4H, *J* = 7.3Hz, CH_2CH_3), 2.45 (d, 4H, *J* = 5.1Hz, CH_2), 1.24(t, 6H, *J* = 7.3Hz, CH_2CH_3), 1.09(s, 3H, CH_3), 1.03(s, 3H, CH_3); ^{13}C NMR

(100 MHz, $CDCl_3$): δ = 198.5, 180.8, 152.5, 142.5, 128.0, 126.7, 125.1, 116.3, 90.9, 51.4, 45.9, 42.2, 33.0, 28.4, 27.6, 11.3; LC/MS (ESI): 429$[M]^+$; Anal. for $C_{23}H_{31}N_3O_5$; calcd: C, 64.32; H, 7.27; N, 9.78;Found: C, 64.29; H, 7.29; N, 9.80.

5-((4-Bromophenyl)(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)methyl)-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (5l)

5l was prepared from barbituric acid **1b**, dimedone **2** and *p*-bromobenzaldehyde **3** according to the general procedure (**GP1**) yielding a white solid material (678 mg, 1.33 mmol, 89%). m.p: 208 °C; IR (KBr, cm^{-1}): 3093, 2939, 2885, 2829, 2551, 1746, 1686, 1576, 1506, 1466, 1416, 1268, 1241; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.31 (s, 1H, OH), 8.67 (brs, 2H, NH), 7.05(m, 4H, Ph), 5.79 (s, 1H, benzyl-H), 2.79(q, 4H, J = 7.3Hz, CH_2CH$_3$), 2.35 (d, 4H, J = 5.1Hz, CH_2), 1.21(t, 6H, J = 7.3Hz, CH_2CH_3), 1.11(s, 3H, CH_3), 1.03(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.5, 180.1, 152.8, 140.5, 131.4, 130.7, 128.7, 128.6, 118.5, 115.6, 91.0, 50.9, 42.8, 31.6, 31.5, 29.2, 28.3, 27.8, 11.3; LC/MS (ESI): 508 $[M]^+$; Anal. for $C_{23}H_{30}BrN_3O_5$; calcd: C, 54.34; H, 5.95; Br, 15.72; N, 8.27;Found: C, 54.35; H, 5.96; Br, 15.69; N, 8.30.

5-((2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)(p-tolyl)methyl)-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (5m)

5m was prepared from barbituric acid **1b**, dimedone **2** and tolualdehyde **3** according to the general procedure (**GP1**) yielding a white solid material (604 mg, 1.36 mmol, 91%). m.p: 213 °C; IR (KBr, cm^{-1}): 3150, 2955, 2867, 1690, 1592, 1508, 1375, 1256, 1232, 1167;^{1}H NMR (400 MHz, $CDCl_3$): δ 13.31 (s, 1H, OH), 8.83 (brs, 2H, NH), 7.27(d, 2H, J = 8.0Hz, Ph), 7.00(d, 2H, J = 8.0Hz, Ph), 5.88 (s, 1H, benzyl-H), 2.83(q, 4H, J = 7.3Hz, CH_2CH$_3$), 2.31 (d, 4H, J = 5.1Hz, CH_2), 2.23 (s, 3H, CH_3), 1.19(t, 6H, J = 7.3Hz, CH_2CH_3), 1.04(s, 3H, CH_3), 1.02(s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 180.1, 152.8, 140.5, 131.4, 130.7, 128.7, 128.6, 118.5, 115.6, 91.0, 50.9, 42.8, 31.6, 31.5, 29.2, 28.3, 27.8, 20.9, 11.3; LC/MS (ESI): 443 $[M]^+$; Anal. for $C_{24}H_{33}N_3O_5$; calcd: C, 64.99; H, 7.50; N, 9.47;Found: C, 64.95; H, 7.49; N, 9.50.

5.2. Biological activity

5.2.1. Procedure for DPPH Radical Scavenging Assay.

DPPH radical scavenging activities of compounds were determined by using the following method.

All test samples (DMSO solution) were allowed to react with stable free radical, 1, 1-diphenyl-2-picrylhydrazyl radical (DPPH, 300 μM in ethanol) *via* incubation for half an hour at 37 ºC. After incubation, decrease in absorption was measured at 515 nm using multiplate reader (Spectra MAX-340). Percent radical scavenging activity by samples was determined in comparison with a DMSO treated control group by using the following formula:

$$\%RSA = 100 - \{(OD\ test\ compound / OD\ control) \times 100\}$$

Where; RSA is radical scavenging activity and A is absorbance

5.2.2. **Procedure for in vitro** β-Glucuronidase inhibition assay

β-Glucuronidase activity was performed in 0.1 M acetate buffer pH 7. The buffer, various concentration of test compounds, and enzyme was incubated at 37 °C for 30 min. Then the 96-well plates were read on SpectraMax plus 384 (Molecular Devices, CA, USA) at 405 nm after the addition of 0.4 mM *p*-nitrophenyl-β-D-glucuronide.

5.2.3. **Procedure for in vitro thymidine phosphorylase inhibition assay**

Thymidine phosphorylase (*E. coli*) inhibition assay was performed spectrophotometrically by using modified protocol by Bera *et al.* In brief, total reaction mixture of 200 µL contained 150 µL of potassium phosphate buffer (pH 7.0, 50 mM), 20 µL of enzyme with concentration of 0.058 unit/well and incubated with 10µL of test compound. The reaction mixture was incubated for 10 min at 30ºC. After incubation, substrate (20 µL, 1.5 mM) was added and change in absorbance was monitored for 10 minutes at 290 nm in microplate reader (Spectramax, molecular devices, CA, USA). 7-Deazaxanthine was used as positive control [Bera *et. al*., 2013].

5.2.4. **Procedure for in vitro alpha- glucosidase inhibition Assay:**

135 µL of 50 mM phosphate saline buffer pH (6.8) was dispend in the 96-well plate. 20 µl of test sample in 70% DMSO dispensed in to the wells. 20 µl of the enzyme was added in to the wells, and the plate was incubated for 15 min. After incubation, pre- read of the plate was taken by the Spectra max. After the pre – read 25 µl of the substrate (ÞNPG) was added and reading were taken on spectra max at 400 nm for 30 minutes. In the end, normal read is taken and the percent inhibition was calculated.

6. Molecular docking studies

To understand the binding interactions of these newly synthesized compounds in the active sites α-glucosidase, thymidine phosphorylase and β-glucuronidase molecular docking was performed using MOE-Dock program. The crystal structure of α-glucosidase is not available yet, so, we used homology model as described in our previous work [2,3]. The crystal structures of thymidine phosphorylase (PDB: 2wk6), and β-glucuronidase (PDB: ID 1BHG) enzymes were obtained from protein data bank. Before docking the structures were checked for missing atoms, bonds and contacts. The energies of the retrieved protein molecules were minimized after the 3D protonation using the default parameters of MOE energy minimization algorithm (gradient: 0.05, Force Field: MMFF94X).

The three dimensional coordinates of the synthesized compounds were constructed using MOE-Builder tool and hydrogen atoms were added. Then, these molecules were energy minimized using the default parameters of MOE energy minimization algorithm (gradient: 0.05, Force Field: MMFF94X). All the minimized molecules were saved in the mdb file format as input file for MOE-Dock in the next step. To find the correct conformations of the ligands and to obtain minimum energy structures, ligands were allowed to be flexible. The top ranked pose of each compound was selected on the basis of docking score (S) for further analysis. At the end of docking, the best conformations on the basis of docking score were analyzed for binding interactions.

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Table 1. Selected geometric parameters (Å, °) of compound **5a**

O1—C1	**1.248 (2)**	**O1—C1—C2**	**118.2 (2)**
O2—C5	1.307 (3)	O1—C1—C6	123.0 (2)
O3—C9	1.235 (3)	O2—C5—C4	116.32 (18)
O4—C13	1.321 (2)	O2—C5—C6	121.3 (2)
O5—N1	1.231 (3)	O3—C9—C8	121.8 (2)
O6—N1	1.224 (3)	O3—C9—C10	118.88 (18)
N1—C15	1.474 (3)	O4—C13—C12	112.08 (18)
N2—C26	1.522 (4)	O4—C13—C8	124.64 (19)
N2—C25	1.473 (4)	N1—C15—C16	114.58 (19)
O5—N1—O6	123.8 (2)	N1—C15—C14	121.1 (2)
O6—N1—C15	118.59 (18)	N2—C25—C24	110.8 (3)
O5—N1—C15	117.56 (19)	N2—C26—C27	111.0 (3)
C25—N2—C26	112.7 (2)		

Table 2. Hydrogen bonding data for compound **5a**

***D*—H···A**	***D*—H**	**H···A**	***D*···A**	***D*—H···A**
O1W—H2OW···O3	0.96 (3)	1.84 (3)	2.738 (2)	156 (3)
N2—H1N2···O1W	1.02 (3)	1.80 (3)	2.778 (3)	161 (3)
O4—H1O4···O2	1.03 (3)	1.46 (3)	2.470 (2)	168 (3)
O1W—H1OW···O2i	0.84 (3)	1.93 (3)	2.753 (2)	166 (3)
N2—H2N2···O1	0.92 (3)	1.88 (3)	2.732 (3)	153 (2)
C17—H17A···O4ii	0.95	2.52	3.194 (3)	128
C21—H21C···O6iii	0.98	2.57	3.504 (3)	159
C22—H22A···O5i	0.98	2.56	3.518 (3)	165

Symmetry codes: (i) −x+1/2, −y+1, z+1/2; (ii) −x, y+1/2, −z+1/2; (iii) −x+1, y−1/2, −z+1/2.

Table 3. Selected geometric parameters (Å, °) of compound **5d**

O1—C1	**1.3235 (16)**	**O1—C1—C6**	**124.68 (12)**
O2—C5	1.2331 (16)	O2—C5—C4	118.71 (12)
O3—C9	1.2947 (17)	O2—C5—C6	122.43 (12)
O4—C13	1.2443 (16)	O3—C9—C10	115.11 (11)
O5—C17	1.3749 (18)	O3—C9—C8	122.25 (12)
O5—C24	1.421 (2)	O4—C13—C8	123.31 (12)
N1—C26	1.487 (2)	O4—C13—C12	117.50 (12)
N1—C27	1.485 (2)	O5—C17—C16	116.01 (13)
C17—O5—C24	116.81 (12)	O5—C17—C18	124.43 (13)
C26—N1—C27	114.21 (12)	N1—C26—C25	109.41 (13)
O1—C1—C2	111.20 (11)	N1—C27—C28	110.88 (14)

Table 4. Hydrogen bonding data for compound **5d**

***D*—H···A**	***D*—H**	**H···A**	***D*···A**	***D*—H···A**
N1—H2N1···O2i	0.95 (2)	2.21 (2)	2.7834 (17)	118.3 (15)
N1—H2N1···O4i	0.95 (2)	1.99 (2)	2.7275 (16)	134.0 (17)
N1—H1N1···O3	0.891 (19)	1.909 (18)	2.7202 (16)	150.6 (17)
O1—H1O1···O3	1.02 (2)	1.46 (2)	2.4641 (14)	166 (2)
C26—H26A···O1	0.99	2.51	3.3374 (17)	142

Symmetry code: (i)−*x*+3/2, *y*−1/2, −*z*+1/2.

Table 5. Selected geometric parameters (Å, °) of compound **5f**

O1—C1	**1.290 (2)**	**O1—C1—C6**	**122.08 (17)**
O2—C5	1.248 (2)	O1—C1—C2	115.39 (14)
O3—C9	1.231 (2)	O2—C5—C4	117.50 (17)
O4—C13	1.334 (2)	O2—C5—C6	123.24 (17)
O5—N1	1.223 (3)	O3—C9—C8	122.20 (17)
O6—N1	1.228 (2)	O3—C9—C10	118.78 (16)
N1—C17	1.467 (3)	O4—C13—C12	111.29 (15)
N2—C25	1.485 (3)	O4—C13—C8	124.54 (17)
N2—C26	1.482 (3)	N1—C17—C16	119.27 (17)
O5—N1—O6	123.56 (18)	N2—C25—C24	110.50 (19)
O6—N1—C17	117.96 (18)	N2—C26—C27	110.30 (18)
O5—N1—C17	118.47 (17)	O2—C5—C4	117.50 (17)
C25—N2—C26	113.86 (16)	O2—C5—C6	123.24 (17)

Table 6. Hydrogen bonding data for compound **5f**

***D*—H···A**	***D*—H**	**H···A**	***D*···A**	***D*—H···*A***
N2—H2N2···O2^{i}	0.87 (2)	2.02 (2)	2.703 (2)	135.3 (19)
N2—H2N2···O3^{i}	0.87 (2)	2.23 (2)	2.806 (2)	124.3 (19)
N2—H1N2···O1	0.91 (3)	1.87 (3)	2.679 (2)	148 (3)
O4—H1O4···O1	0.95 (3)	1.55 (3)	2.4886 (19)	166 (3)
C10—H10A···O6^{ii}	0.99	2.53	3.402 (2)	146
C16—H16A···O2^{iii}	0.95	2.57	3.517 (2)	176
C26—H26A···O6^{iv}	0.99	2.60	3.539 (3)	159

Symmetry codes: (i) −*x*+1/2, *y*+1/2, −*z*+3/2; (ii) −*x*+1, −*y*+1, −*z*+1; (iii) −*x*, −*y*+1, −*z*+1; (iv) *x*+1/2, −*y*+3/2, *z*+1/2.