Supplemental section

Novel 3,5-bis(arylidene)-4-oxo-1-piperidinyl dimers: structure-activity relationships and potent antileukemic and antilymphoma cytotoxicity

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Characterization of 3,5-bis(arylidene)-4-piperidone dimers (3a-i, 4a-i and 5)

Melting points were determined on a Gallenkamp instrument and are uncorrected. ^{1}H and ^{13}C NMR were recorded using a Bruker Avance 500 MHz spectrometer equipped with a 5mm BBO probe. Chemical shifts (δ) are reported in ppm. Elemental analyses were undertaken using an Elementer CHNS analyzer. The ^{1}H and ^{13}C NMR spectra of three representative compounds (one from each series) namely **3e**, **4e** and **5** are presented.

*1,2-bis[3,5-bis(Benzylidene)-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3a**)*[1]

Yield: 62%; mp (chloroform/methanol) 246 ^{o}C; ^{1}H NMR(500 MHz, DMSO-d_6): δ 7.72(s, 2H, 2×=CH), 7.56 (s, 2H, 2×=CH), 7.53(t, 4H, Ar-H), 7.49(d, J=7.07 Hz, 2H, Ar-H), 7.45(m, 6H, Ar-H), 7.39(m, 8H, Ar-H), 4.48(d, J=23.28Hz, 8H, 4×NCH_2; ^{13}C NMR (125MHz, DMSO-d_6):184.7, 162.6, 137.9, 137.5, 134.4, 134.1, 131.4, 131.0, 130.9, 130.7, 130.2, 130.1, 129.3, 129.2, 46.4, 41.6,; MS (ESI) m/z: 627 $(M+Na)^{+}$. Anal.calcd for $C_{40}H_{32}N_2O_4.H_2O$: C 77.17; H 5.14; N 4.50, found: C 77.05; H 4.87; N 4.42.

*1,2-bis[3,5-bis(4-Fluorobenzylidene)-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3b**)*[2]

Yield: 67%; mp (chloroform/methanol) 253 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73(s, 2H, 2×=CH), 7.57 (s, 2H, 2×=CH), 7.37(q, 4H, Ar-H), 7.25 (q, 4H, Ar-H), 7.18 (t, 4H, Ar-H), 7.098(t, 4H, Ar-H), 4.63 (s, 4H, 2×NCH_2), 4.51 (s, 4H, 2×NCH_2). Anal.calcd for $C_{41}H_{26}Cl_8N_2O_4.H_2O$: C 53.93; H 3.09; N 3.07 %, found: C 53.84; H 2.98; N 2.74%.

*1,2-bis[3,5-bis(4-Chlorobenzylidene)-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3c**)*[2]

Yield: 61%; mp (methanol) 289 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72(s, 2H, 2×=CH), 7.54 (s, 2H, 2×=CH), 7.46 (d, J=8.40 Hz, 2H, Ar-H), 7.37(d, J=8.37 Hz, 2H, Ar-H), 7.31(d, J=8.42 Hz, 4H, Ar-H), 7.20(d, J=8.38 Hz, 4H, Ar-H), 4.62 (s, 4H, 2×NCH_2), 4.52 (s, 4H, 2×NCH_2). Anal.calcd for $C_{40}H_{28}Cl_4N_2O_4.3\ H_2O$: C 60.26; H 3.54; N 3.51 %, found: C 60.35; H 3.70; N 3.15%.

*1,2-bis[3,5-bis(3,4-Dichlorobenzylidene)-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3d**)*[2]

Yield: 64%; mp (chloroform/methanol) 271 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (s, 2H, 2×=CH), 7.55 (s, 1H, =CH), 7.53 (s, 1H, =CH), 7.46 (d, J=8.15 Hz, 6H, Ar-H), 7.41(d, J=1.71

Hz, 2H, Ar-H), 7.20 (dd, J=1.67Hz, J=1.71Hz, 2H, Ar-H), 7.05 (dd, J=1.71 Hz, J=1.77 Hz, 2H, Ar-H), 4.67 (s, 4H, 2×NCH_2), 4.56 (s, 4H, 2×NCH_2). Anal.calcd for $C_{40}H_{24}Cl_8N_2O_4$: C 54.58; H 2.75; N 3.18 %, found: C 54.52; H 2.90; N 2.95 %.

*1,2-bis[3,5-bis(4-Methylbenzylidene)-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3e**)*[2]

Yield: 53%; mp (chloroform/methanol) 275 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79(s, 2H, 2×=CH), 7.65 (s, 2H, 2×=CH), 7.29 (d, J=7.70 Hz, 8H, Ar-H), 7.18(q, 8H, Ar-H), 4.53 (d, J=15.61 Hz, 8H, 4×NCH_2), 2.44 (s, 6H, 2×CH_3), 2.28 (s, 6H, 2×CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 185.04(CO), 162.73(CON), 140.31(C=C-Ph), 140.22(C=C-Ph), 139.15(C=C-Ph), 138.29(C=C-Ph), 131.57(Ar-C),131.07(Ar-C), 130.67(Ar-C), 130.33(Ar-C), 129.72(Ar-C), 129.62(Ar-C), 129.46(Ar-C), 129.00(Ar-C), 46.07(CH_2NCO), 42.05(CH_2NCO), 21.53(CH_3), 21.43(CH_3). Anal.calcd for $C_{44}H_{40}N_2O_4$.1.5 H_2O: C 76.76; H 6.30; N 4.07 %, found: C 76.46; H 6.39; N 3.93%.

*1,2-bis[3,5-bis(3,4-Dimethoxybenzylidene)-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3f**)*[2]

Yield: 60%; mp (chloroform/methanol) 282 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71(s, 2H, 2×=CH), 7.42 (s, 2H, 2×=CH), 6.99 (d, J=8.47 Hz, 4H, Ar-H), 6.94(d, J=8.08 Hz, 2H, Ar-H), 6.80(m, 6H, Ar-H), 4.70 (s, 4H, 2×NCH_2), 4.64 (s, 4H, 2×NCH_2), 4.00 (s, 6H, 2×OCH_3), 3.96 (d, 12H, 4×OCH_3), 3.74 (s, 6H, 2×OCH_3). Anal.calcd for $C_{48}H_{48}N_2O_{12}$.H_2O: C 66.75; H 5.84; N 3.24 %, found: C 66.31; H 5.62; N 3.06%.

*1,2-bis[3,5-bis(3,4,5-Trimethoxybenzylidene)-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3g**)*[2]

Yield: 57%; mp (ethanol) 273 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63(s, 2H, 2×=CH), 7.44 (s, 2H, 2×=CH), 6.66 (s, 4H, Ar-H), 6.49 (s, 4H, Ar-H), 4.75 (s, 4H, 4×NCH_2), 4.68 (s, 4H, 4×NCH_2), 3.96 (s, 12H, 4×OCH_3), 3.94 (s, 9H, 3×OCH_3), 3.88 (s, 9H, 3×OCH_3), 3.84 (s, 6H, 2×OCH_3). Anal.calcd for $C_{52}H_{56}N_2O_{16}$: C 64.72; H 5.85; N 2.90 %, found: C 64.95; H 6.16; N 2.78%.

*1,2-bis[3,5-bis(4-Methoxybenzylidene)-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3h**)*[2]

Yield: 71%; mp (chloroform/methanol) >300 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74(s, 2H, 2×=CH), 7.58 (s, 2H, 2×=CH), 7.35 (d, J=8.65 Hz, 4H, Ar-H), 7.22 (d, J=8.63 Hz, 4H, Ar-H),

6.98 (d, J=8.71 Hz, 4H, Ar-H), 6.91 (d, J=8.67 Hz, 4H, Ar-H), 4.60 (s, 4H, 2×NCH_2), 4.53 (s, 4H, 2×NCH_2), 3.90 (s, 6H, 2×OCH_3), 3.76 (s, 6H, 2×OCH_3). Anal.calcd for $C_{44}H_{40}N_2O_8$: C 72.91; H 5.56; N 3.86 %, found: C 72.57; H 5.94; N 3.75%.

*1,2-bis[3,5-bis{4-(N,N-Dimethylamino)benzylidene}-4-oxo-piperidin-1-yl]ethane-1,2-dione (**3i**)*[2]

Yield: 46%; mp (chloroform/methanol) >300 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75(s, 2H, 2×=CH), 7.65 (s, 2H, 2×=CH), 7.33 (d, J=8.75 Hz, 4H, Ar-H), 7.21(d, J=8.71 Hz, 4H, Ar-H), 6.73 (d, J=16.93 Hz, 8H, Ar-H), 4.58 (s, 4H, 2×NCH_2), 4.54 (s, 4H, 2×NCH_2), 3.08 (s, 12H, 4×NCH_3), 2.95 (s, 12H, 4×NCH_3). Anal.calcd for $C_{44}H_{40}N_2O_4.1.5\ H_2O$: C 76.76; H 6.30; N 4.07 %, found: C 76.46; H 6.39; N 3.93%.

*1,3-bis-[3,5-bis(Benzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4a**)*[1]

Yield: 65%; mp (acetone) 201 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.72(s, 2H, 2×=CH), 7.57(s, 2H, 2×=CH), 7.53(d, J=4.18Hz, 8H, Ar-H), 7.47 (m, 12H, Ar-H), 4.62(d, J=21.13Hz, 8H, 4×NCH_2), 3.46(s, 2H, CH_2); ^{13}C NMR (125MHz, DMSO-d_6):186.3, 165.9,136.6, 136.5, 134.7, 134.5, 132.6, 132.5, 131.0, 130.9, 130.1, 130.0, 129.3, 129.2, 47.0, 42.4; MS (ESI) m/z: 641 $(M+Na)^+$. Anal.calcd for $C_{41}H_{34}N_2O_4.H_2O$: C 77.27; H 5.65; N 4.39, found: C 77.31; H 5.50; N 4.47.

*1,3-bis-[3,5-bis(4-Fluorobenzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4b**)*[2]

Yield: 56%; mp (chloroform/methanol) >300 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (s, 2H, 2×=CH), 7.75 (s, 2H, 2×=CH), 7.49(q, 4H, Ar-H), 7.33 (q, 4H, Ar-H), 7.18 (t, 4H, Ar-H), 7.12 (t, 4H, Ar-H), 4.84 (s, 4H, 2×NCH_2), 4.79 (s, 4H, 2×NCH_2), 3.22 (s, 2H, CH_2). Anal.calcd for $C_{41}H_{30}F_4N_2O_4.H_2O$: C 69.42; H 4.27; N 3.95 %, found: C 69.58; H 4.30; N 3.71%.

*1,3-bis-[3,5-bis(4-Chlorobenzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4c**)*[2]

Yield: 58%; mp (chloroform/methanol) 260 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.64 (s, 2H, 2×=CH), 7.60 (s, 2H, 2×=CH), 7.57 (d, J=11.46 Hz, 4H, Ar-H), 7.54 (d, J=7.60 Hz, 4H, Ar-H), 7.49 (q, 8H, Ar-H), 4.62 (d, 8H, J=10.15 Hz, 4×NCH_2), 3.51 (s, 2H, CH_2). Anal.calcd for $C_{41}H_{30}Cl_4N_2O_4.2.5\ H_2O$: C 61.38; H 3.77; N 3.49 %, found: C 61.10; H 3.69; N 3.30%.

*1,3-bis-[3,5-bis(3,4-Dichlorobenzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4d**)*[2]

Yield: 65%; mp (chloroform/methanol) 236 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (s, 2H, 2×=CH), 7.63 (s, 2H, 2×=CH), 7.56 (q, 8H, Ar-H), 7.51 (d, J=8.29 Hz, 2H, Ar-H), 7.30 (d, J=1.45 Hz, 2H, Ar-H), 7.31 (dd, J=1.45 Hz, J=1.53 Hz, Ar-H), 7.15 (dd, J=1.48 Hz, 2H, Ar-H), 4.78 (d, 8H, J=6.72 Hz, 4×NCH_2), 3.30 (s, 2H, CH_2). Anal.calcd for $C_{41}H_{26}Cl_8N_2O_4$. H_2O: C 53.93; H 3.09; N 3.07 %, found: C 53.84; H 2.98; N 2.74%.

*1,3-bis-[3,5-bis(4-Methylbenzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4e**)* [2]

Yield: 43%; mp (chloroform/methanol) 251 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (s, 2H, 2×=CH), 7.74 (s, 2H, 2×=CH), 7.40 (d, J=7.90 Hz, 4H, Ar-H), 7.27 (d, J=7.60 Hz, 4H, Ar-H), 7.21(q, 8H, Ar-H), 4.89 (s, 4H, 2×NCH_2), 4.65 (s, 4H, 2×NCH_2), 3.15 (s, 2H, CH_2), 2.43 (s, 6H, 2×CH_3), 2.41(s, 6H, 2×CH_3). ^{13}C NMR (125MHz, $CDCl_3$): δ 186.39(CO), 165.30(CON), 140.31(C=C-Ph), 140.17(C=C-Ph), 138.62(C=C-Ph), 137.34(C=C-Ph), 131.86(Ar-C), 131.39(Ar-C), 130.88(Ar-C), 130.53(Ar-C), 130.45(Ar-C), 130.39(Ar-C), 130.33(Ar-C), 129.68(Ar-C), 129.61(Ar-C), 128.77(Ar-C), 46.79(CH_2NCO), 43.85(CH_2NCO), 40.54 ($COCH_2CO$), 21.53(CH_3). Anal.calcd for $C_{45}H_{42}N_2O_4.H_2O$: C 77.94; H 6.40; N 4.04 %, found: C 77.94; H 6.63; N 3.98%.

*1,3-bis-[3,5-bis(3,4-Dimethoxybenzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4f**)* [2]

Yield: 65 %; mp (chloroform/methanol) >300 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.86 (s, 4H, 4×=CH), 7.17 (s, 4H, Ar-H), 7.13 (s, 8H, Ar-H), 4.54 (s, 8H, 4×NCH_2), 3.84 (d, J=7.27 Hz, 24H, 8×OCH_3), 3.48 (s, 2H, CH_2). Anal.calcd for $C_{49}H_{50}N_2O_{12}$.7 H_2O: C 59.69; H 6.54; N 2.84 %, found: C 59.82; H 6.18; N 2.71%.

*1,3-bis-[3,5-bis(3,4,5-Trimethoxybenzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4g**)* [2]

Yield: 53%; mp (chloroform/methanol) 115 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (s, 2H, 2×=CH), 7.74 (s, 2H, 2×=CH), 6.72 (s, 4H, Ar-H), 6.58 (s, 4H, Ar-H), 4.96 (s, 4H, 2×NCH_2), 4.90 (s, 4H, 2×NCH_2), 3.92 (d, J=15.37 Hz, 30H, 10×OCH_3), 3.86 (s, 6H, 2×OCH_3), 3.37 (s, 2H, CH_2). Anal.calcd for $C_{53}H_{58}N_2O_{16}.H_2O$: C 63.83; H 6.07; N 2.81 %, found: C 63.84; H 6.27; N 2.51%.

*1,3-bis-[3,5-bis(4-Methoxybenzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4h**)* [2]

Yield: 61%; mp (chloroform/methanol) 245 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (s, 2H, 2×=CH), 7.73 (s, 2H, 2×=CH), 7.48 (d, J=8.6 Hz, 4H, Ar-H), 7.29 (d, J=10.17 Hz, 2H, Ar-H), 6.98 (d, J=8.49 Hz, 4H, Ar-H), 4.85(s, 4H, 2×NCH_2), 4.72 (s, 4H, 2×NCH_2), 3.88 (d, J=7.72 Hz, 12H, 4×OCH_3), 3.22 (s, 2H, CH_2). Anal.calcd for $C_{45}H_{42}N_2O_8$.4 H_2O: C 66.59; H 5.22; N 3.45 %, found: C 66.68; H 5.38; N 3.27%.

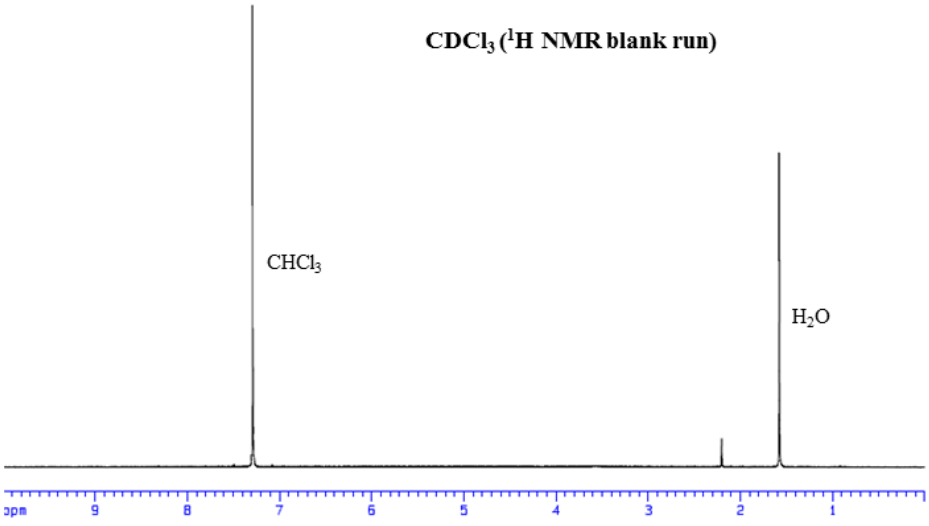
*1,3-bis-[3,5-bis(4-Hydroxybenzylidene)-4-oxo-piperidin-1yl]propane-1,3-dione (**4i**)*[2]

Yield: 56%; mp (chloroform/ethanol) >300 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.64 (s, 2H, 2×=CH), 7.60 (s, 2H, 2×=CH), 7.57 (d, J=11.46 Hz, 4H, Ar-H), 7.54 (d, J=7.60 Hz, 4H, Ar-H), 7.49 (q, 8H, Ar-H), 4.62 (d, 8H, J=10.15 Hz, 4×NCH_2), 3.51 (s, 2H, CH_2). Anal.calcd for $C_{41}H_{34}N_2O_8$.4.5 H_2O: C 64.46; H 5.68; N 3.67 %, found: C 64.59; H 5.31; N 3.59%.

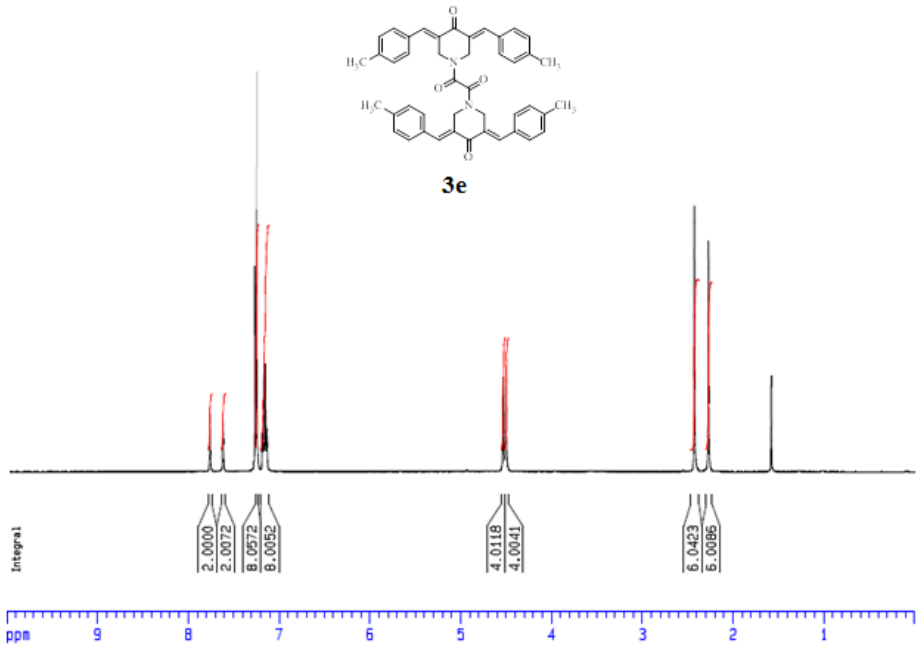
*1,3-bis-[3,5-bis(benzylidene)-4-oxo-piperidin-1yl]propane (**5**)*[2]

Yield: 63 %; mp (acetone) 135 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81(s, 4H, 4×=CH), 7.39 (m, 20H, Ar-H), 3.78 (s, 8H, 4×NCH_2), 2.54 (t, 4H, 2×CH_2), 1.60 (p, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.34 (<u>C</u>O), 136.57 (C=<u>C</u>-Ph), 135.20 (C=<u>C</u>-Ph), 133.11 (<u>C</u>=C-Ph), 130.40 (Ar-C), 129.05 (Ar-C), 128.60(Ar-C), 55.38 (N<u>C</u>$H_2$$CH_2$), 54.97 (N<u>C</u>$H_2$-piperidone), 25.91 (<u>C</u>H_2). Anal.calcd for $C_{41}H_{38}N_2O_2$: C 83.36; H 6.48; N 4.74 %, found: C 83.74; H 6.79; N 5.05%.

<u>^{1}H and ^{13}C NMR spectra for representative compounds from the series 3-5</u>



^{1}H NMR



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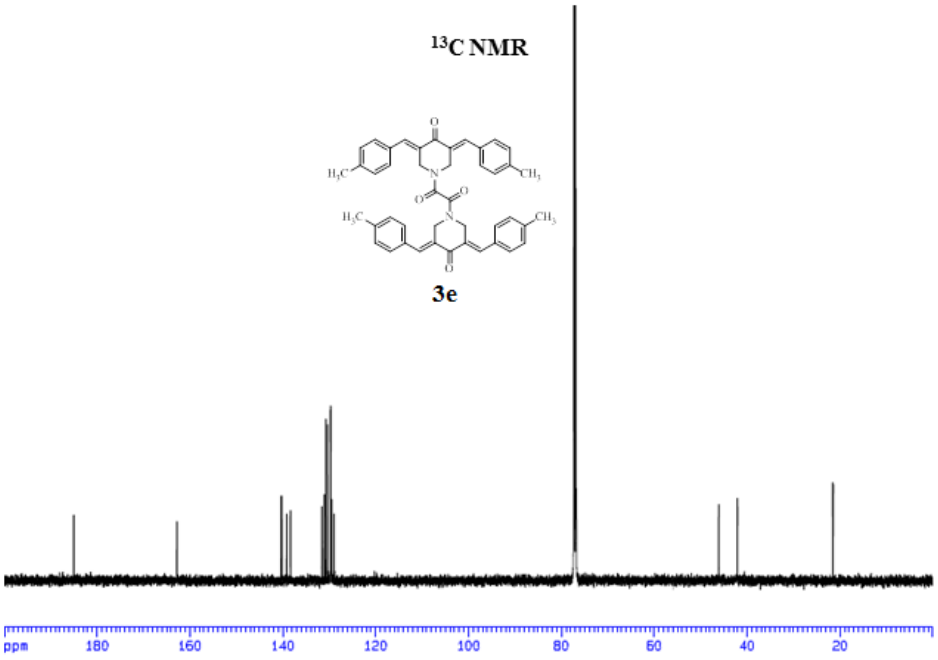

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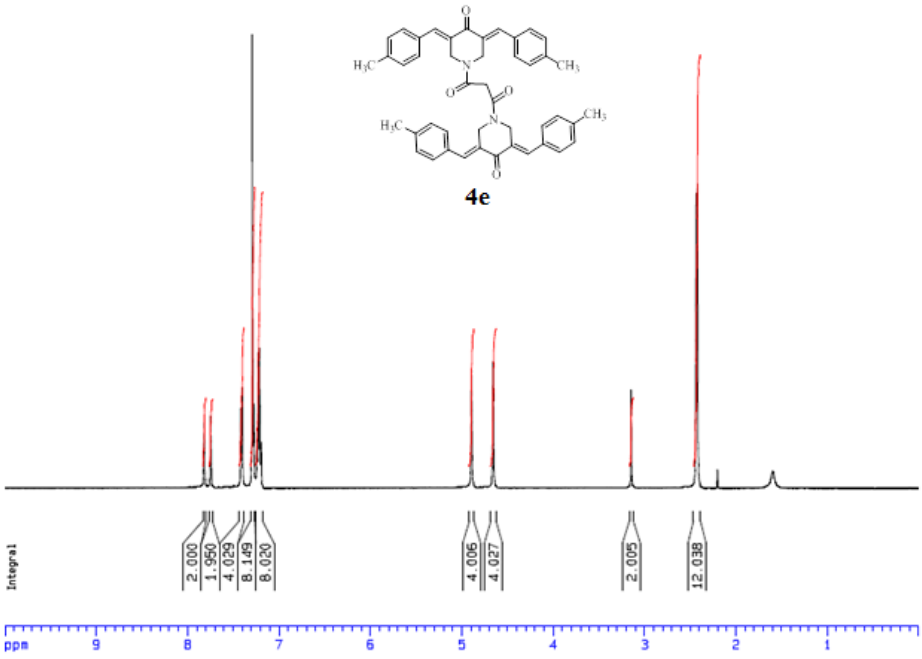

4e

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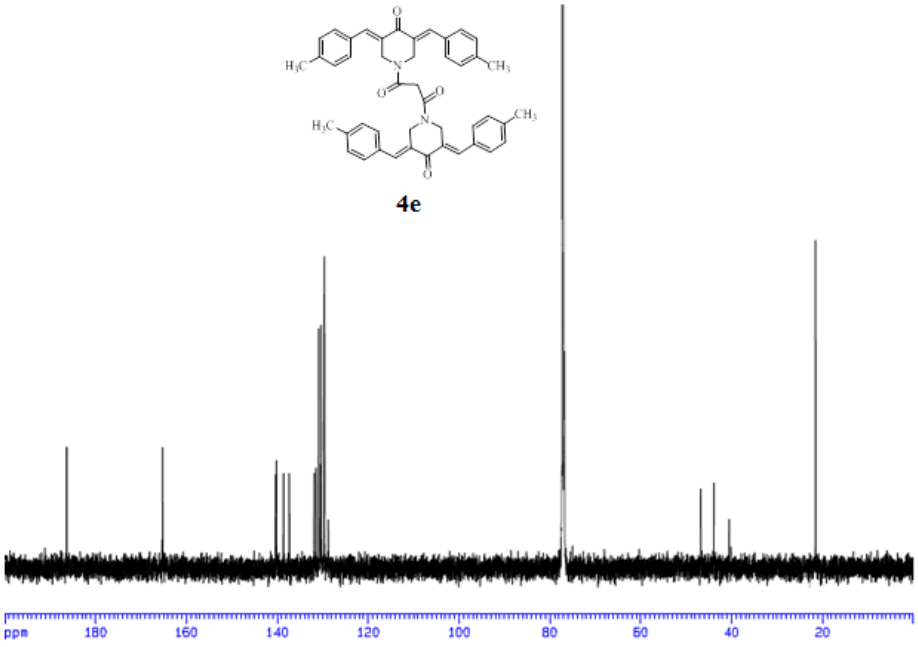
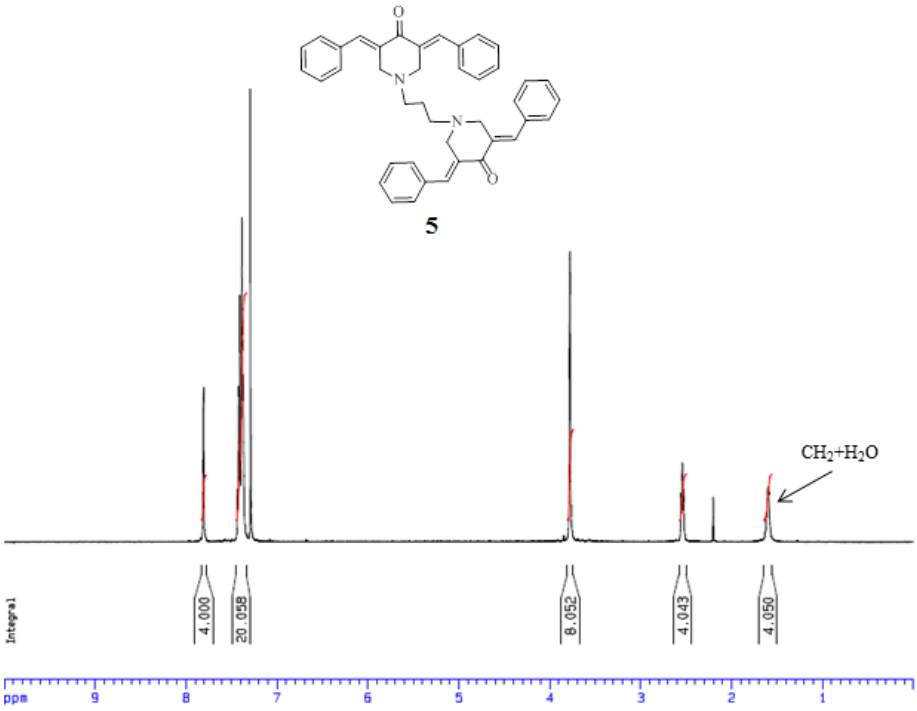
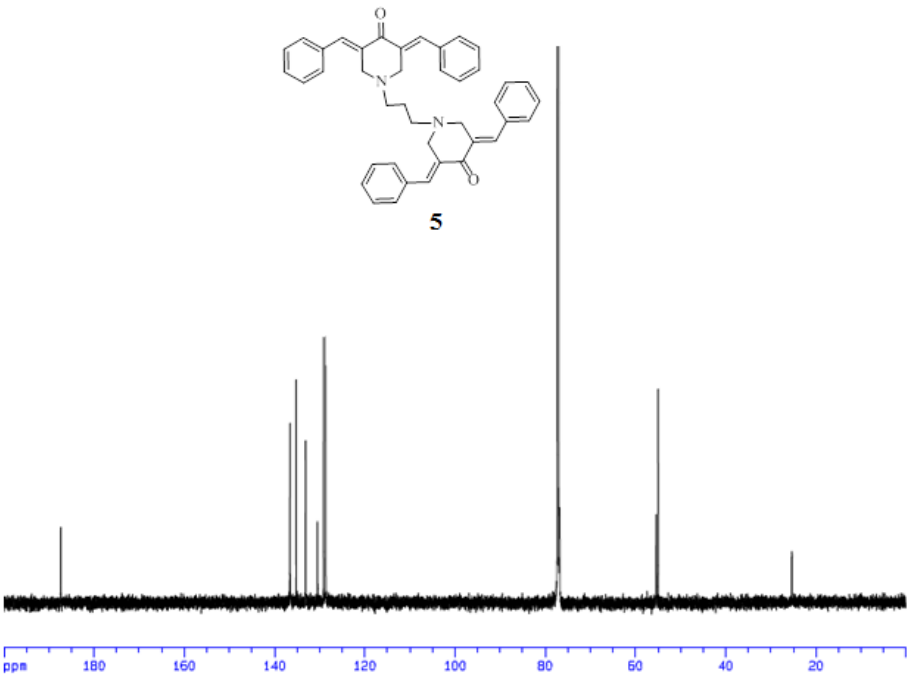


4e

^{1}H NMR



^{13}C NMR



Kendall's coefficient of concordance

The equation used to obtain the coefficient of concordance is derived as follows. In this case the cytotoxin i is given the rank r_{ij} where j is the cell line, and there are N cytotoxins and M cell lines. Thus the total rank R given to cytotoxin i is $R_i = \sum_{j=1}^{M} r_{i,j}$, and the mean value of these ranks is $\bar{R} = \frac{1}{2}m(n+1)$.

The sum of the squared deviations, (S), is defined as: $\sum_i^N (R_i - \bar{R})^2$.

Kendall's coefficient of concordance (W) is: $W = \frac{12S}{M^2(N^3-N)}$. …(1) If all the cell lines produce identical rankings, then W is 1. If there is no agreement, then W is 0.

When two or more compounds have the potencies (i.e., there are ties in the rankings), then equation 1 will understate the degree of concordance and must be adjusted. The correction factor (T_j) is defined as $T_j = \sum_{t=1}^{g_j} (t_i^3 - t_i)$, in which ti is the number of tied ranks in the ith group of tied ranks (the number of cases of equal potency at a specific IC_{50} value) and g_j is the number of tie values. If there are no tied ranks for cell line j then this will be 0. Using this correction for ties, Kendall's coefficient of concordance as: $W = \frac{12\sum_{i=1}^{N}(R_i^2) - 3M^2N(N+1)^2}{M^2N(N^2-1) - M\sum_{j=1}^{M}(T_j)}$ …(2)

Table 1. Evaluation of **3b,c,e-h**, **4b,c,e,f** and **5** against various lymphoma and leukemic cell lines[a]

	% dead cells											
Compound	Jurkat	CEM	SUP-T	HUT-102	Molt-3	EL-4	Nalm-6	Raji	Ramos	BJAB	YT	Average
3b	87.8	85.3	35.6	64.4	3.1	34.7	61.6	33.5	53.3	61.8	17.1	48.9
3c	78.5	59.9	18.1	31.4	0.4	52.5	59.0	35.7	82.9	43.1	21.5	43.9
3e	80.7	68.4	18.8	13.9	0.8	43.5	59.5	41.5	84.4	41.5	20.1	43.0
3f	84.8	88.1	33.0	50.9	31.8	46.5	60.7	56.3	87.4	62.8	39.2	58.3
3g	78.7	84.1	38.2	50.5	30.3	33.8	67.6	55.7	65.1	60.9	13.0	52.5
3h	72.0	71.9	15.2	6.7	49.6	71.7	62.6	69.1	53.7	45.8	5.8	47.7
4b	87.1	92.4	24.9	58.5	2.6	47.7	51.9	35.3	78.6	61.2	19.2	50.9
4c	85.3	83.0	21.1	20.4	20.6	55.4	68.6	32.7	86.3	49.9	16.8	49.1
4e	85.5	85.7	23.6	50.9	21.3	66.9	67.6	46.5	83.0	60.2	29.1	56.4
4f	83.9	77.6	31.0	51.6	2.6	43.7	63.9	50.8	88.6	61.0	32.3	53.4
5	76.3	64.5	21.2	10.0	27.4	65.3	49.2	31.9	82.1	39.4	6.6	43.1
Average	81.9	78.3	25.5	37.2	17.3	51.1	61.1	44.5	76.9	53.4	20.1	49.8

[a]A concentration of 1 μM of each compound was incubated with different cell lines for 24 h at 37° C. The figures of the percentage of dead cells are the average of three independent experiments.

Table 2. Evaluation of **3b,c,e-h**, **4b,c,e,f** and **5** against some breast and prostate cancer cells and nonmalignant cells[a]

	% dead cells									
Compound	MCF-7	MDA231	HCC70	Average	MCF10A	DU145	22rv1	LAPC4	Average	Hs-27
3b	16.2	5.5	6.6	9.43	7.7	15.2	30.1	11.3	18.9	0.6
3c	17.8	10.0	8.4	12.1	2.2	33.1	13.6	27.0	24.6	0.0
3e	0.0	9.3	11.9	7.07	9.3	26.0	16.2	2.4	14.9	12.0
3f	17.7	4.6	3.9	8.73	5.8	45.7	38.2	35.4	39.8	10.2
3g	43.2	4.7	7.3	18.4	7.6	41.3	3.4	9.7	18.1	15.4
3h	16.2	0.6	14.7	10.5	9.9	11.4	0.0	1.9	4.43	0.6
4b	0.2	0.4	3.1	1.23	7.0	38.4	18.8	11.1	22.8	0.3
4c	19.5	32.7	7.8	20.0	3.1	40.3	1.7	1.0	14.3	5.7
4e	19.1	8.6	10.1	12.6	15.4	21.9	6.3	7.0	11.7	26.5
4f	23.0	1.8	2.1	8.97	6.1	67.4	2.0	20.6	30.0	6.4
5	43.5	20.1	4.3	22.6	19.4	19.4	1.7	5.7	8.93	2.9
Average	19.7	8.94	7.29	11.9	8.50	32.7	12.0	12.1	19.7	7.33

[a] A concentration of 1 μM of each compound was incubated with different cell lines for 24 h at 37° C. The figures of the percentage of dead cells are the average of three independent experiments.

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