Supporting Information

A Fundamental Relationship between Hydrophobic Properties and Biological Activity for the Duocarmycin SA Class of DNA Alkylating Antitumor Drugs: Hydrophobic Binding-Driven-Bonding

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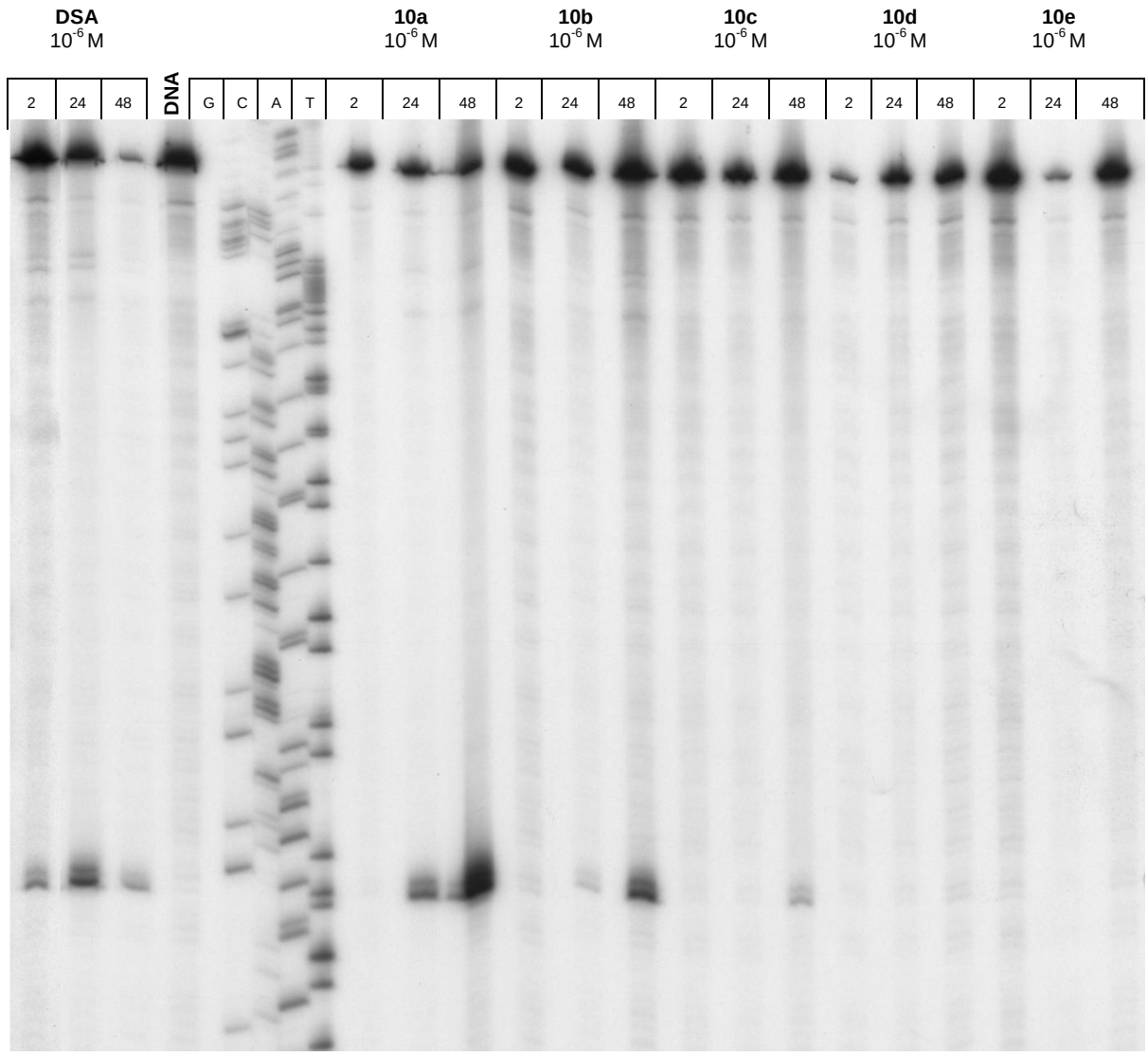

Figure S1. Thermally induced strand cleavage of w794 DNA following DNA alkylation; DNA−agent incubation at 23 °C for 2, 24, and 48 h, removal of unbound agent by EtOH precipitation, and 30 min of thermolysis (100 °C) followed by 8% denaturing PAGE and autoradiography. Lanes 1−3 duocarmycin SA (1×10^{-6}); lane 4, control DNA; lanes 5−8, Sanger G, C, A, and T sequencing reactions; lanes 9−11, **10a** (1×10^{-6}); lanes 12−14, **10b** (1×10^{-6}); lanes 15−17, **10c** (1×10^{-6}); lanes 18−20, **10d** (1×10^{-6}); lanes 21−23, **10e** (1×10^{-6}).

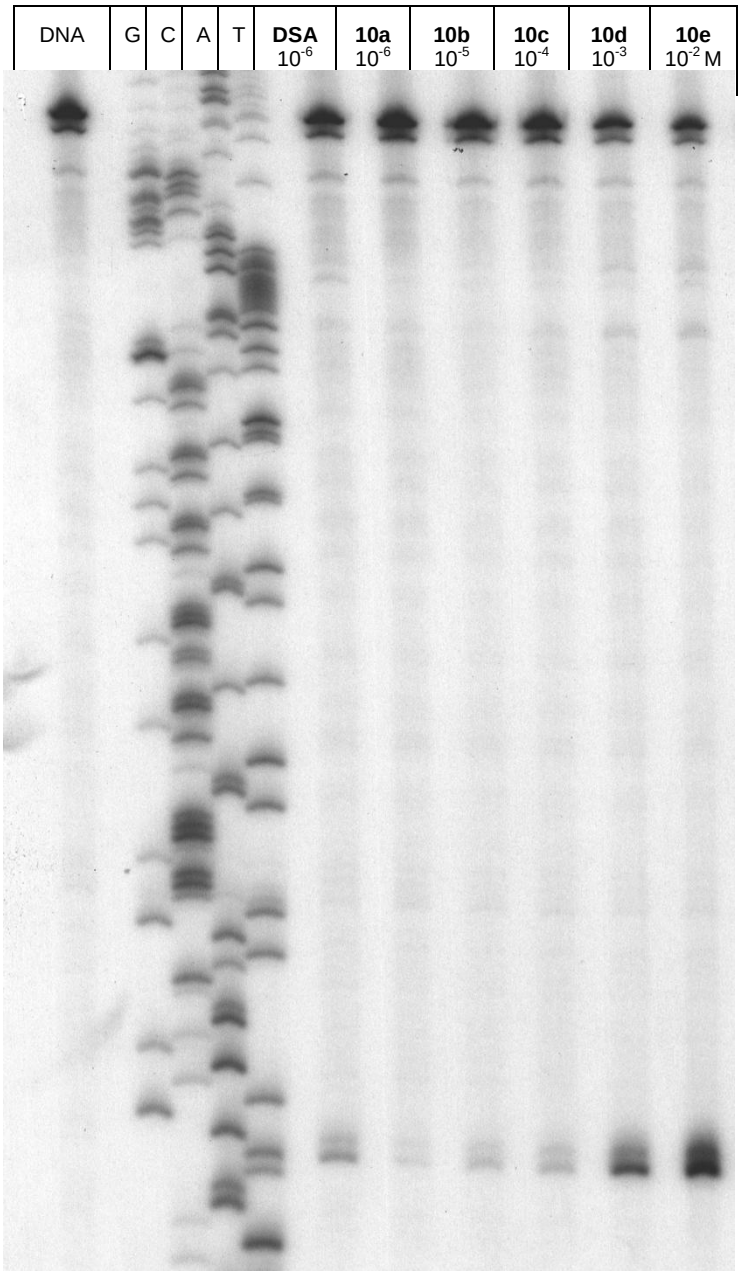

Figure S2. Thermally induced strand cleavage of w794 DNA; DNA−agent incubation at 23 °C for 2 h, removal of unbound agent by EtOH precipitation, and 30 min of thermolysis (100 °C) followed by 8% denaturing PAGE and autoradiography. Lane 1 control DNA; lanes 2−5, Sanger G, C, A, and T sequencing reactions; lane 6, duocarmycin SA (1×10^{-6}); lane 7, **10a** (1×10^{-6}); lane 8, **10b** (1×10^{-5}); lane 9, **10c** (1×10^{-4}); lane 10, **10d** (1×10^{-3}); lane 11, **10e** (1×10^{-2}).

compound	IC_{50} (pM, HCT116)	cLogP
(+)-*seco*-DSA	50	2.44
15a	75	2.33
15b	87	2.20
15c	195	2.06
15d	310	1.93
15e	466	1.79

Table S1. Cell growth inhibition (HCT116) and cLogP for *seco*-duocarmycin SA and **15a**–**e**.

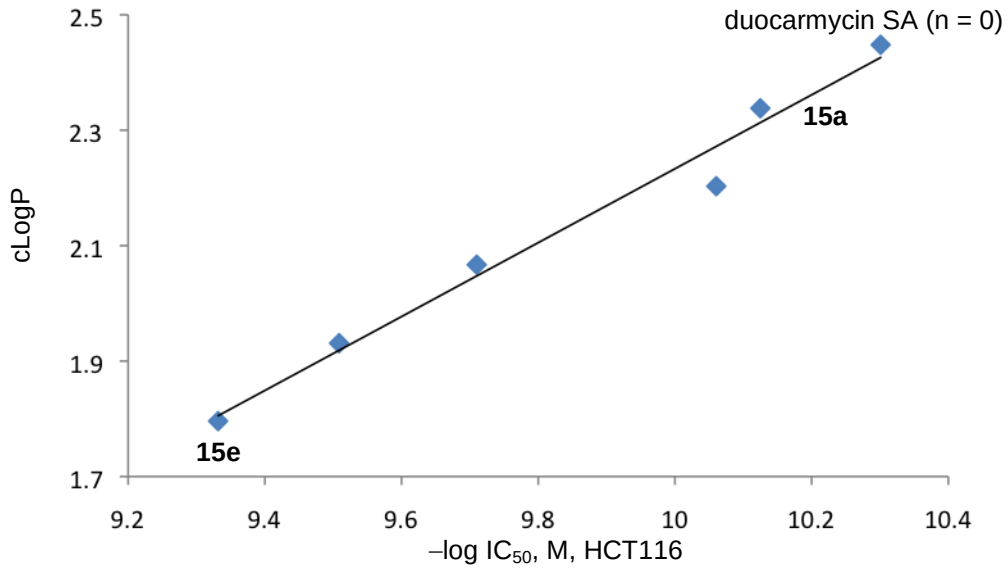

Figure S3. Plot of –log IC_{50} of **2** and **15a-15e** (HCT116) versus cLogP, $r^2 = 0.98$.

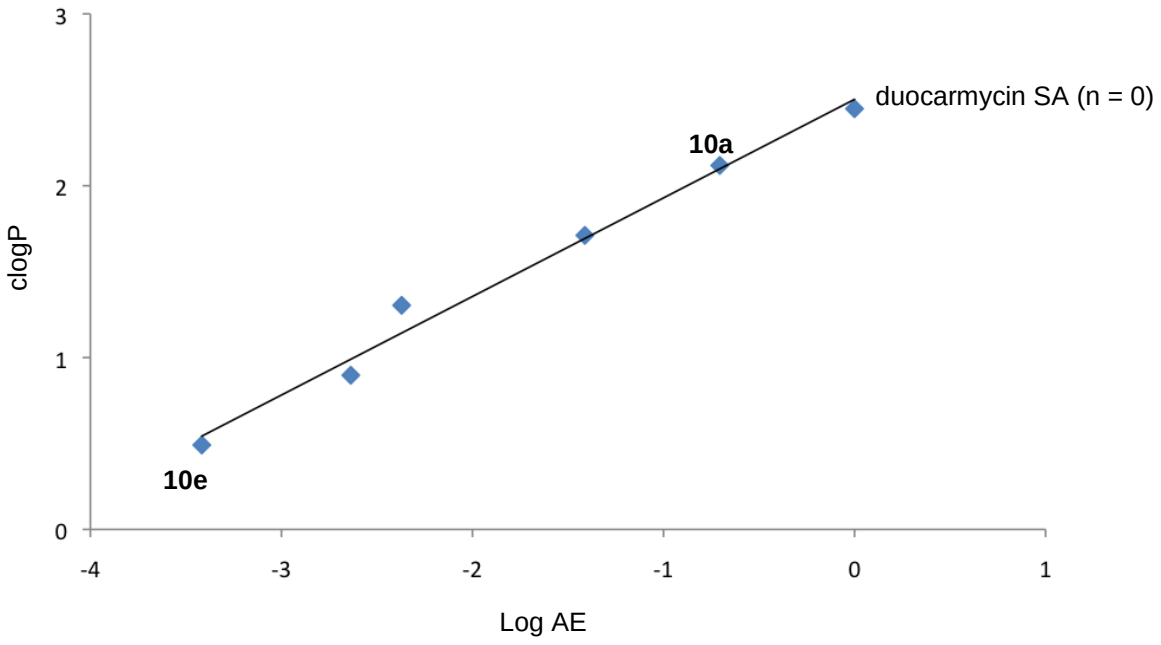

Figure S4. Plot of log AE vs cLogP for **2** and **10a-e** using densitometry values from alkylation cleavage band, $r^2 = 0.98$. Compare to Fig. 8 with values taken from unreacted full length DNA.

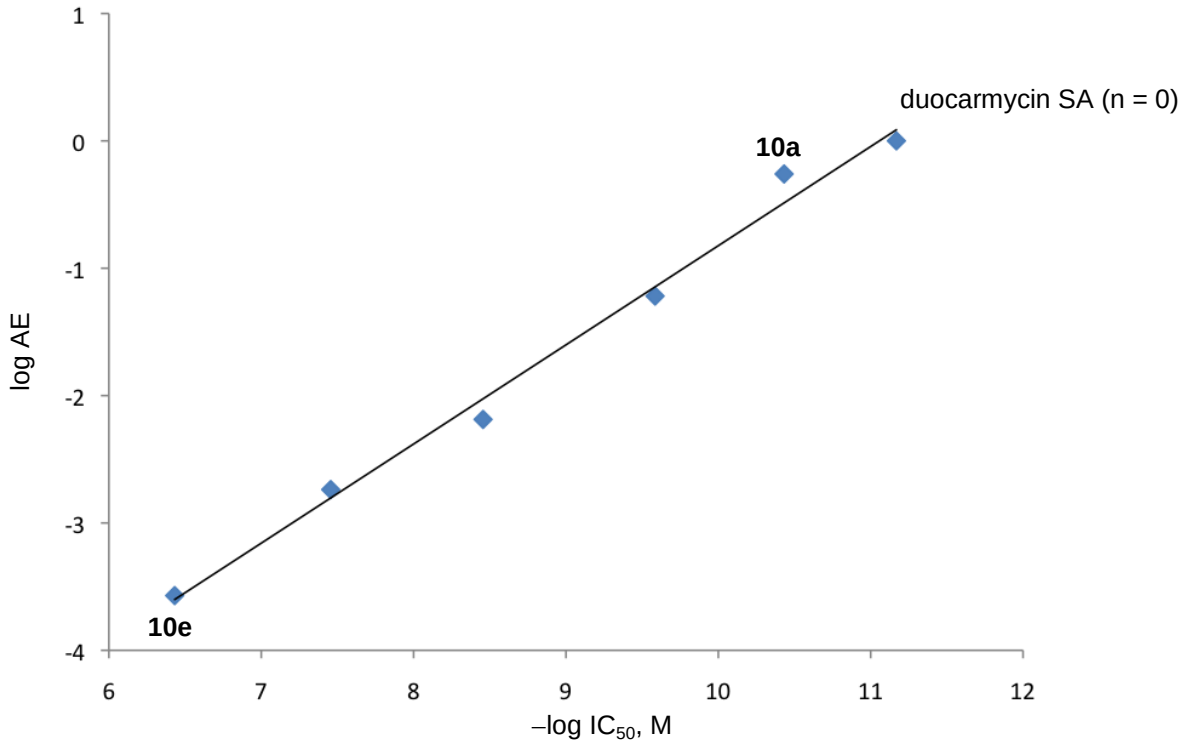

Figure S5. Plot of –log IC_{50} versus log AE (averaged) for **2** and **10a-e**, slope = 0.85, $r^2 = 0.99$.