Figure 1. Synthetic Scheme of Linker **1b** and Dimers **1d-g**

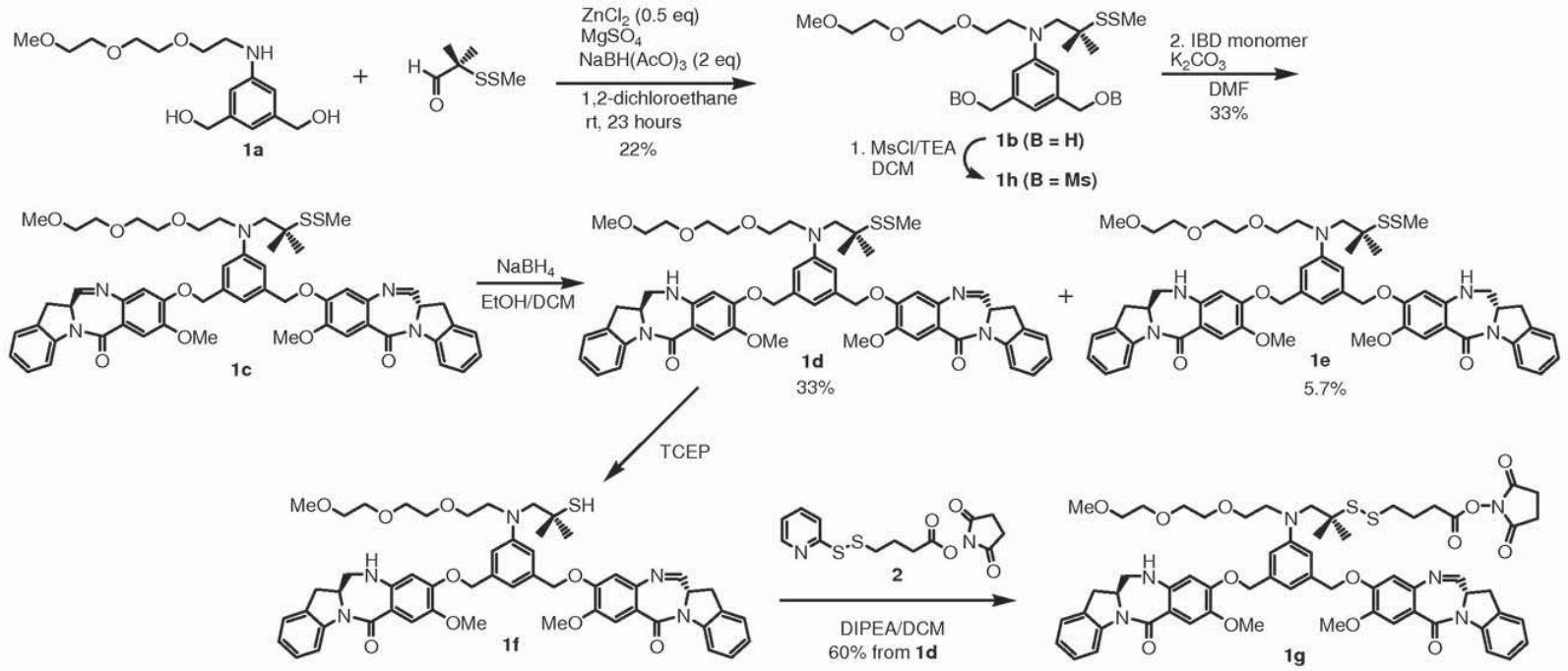


Figure 2. Synthetic Scheme of Dimers **2a-b**

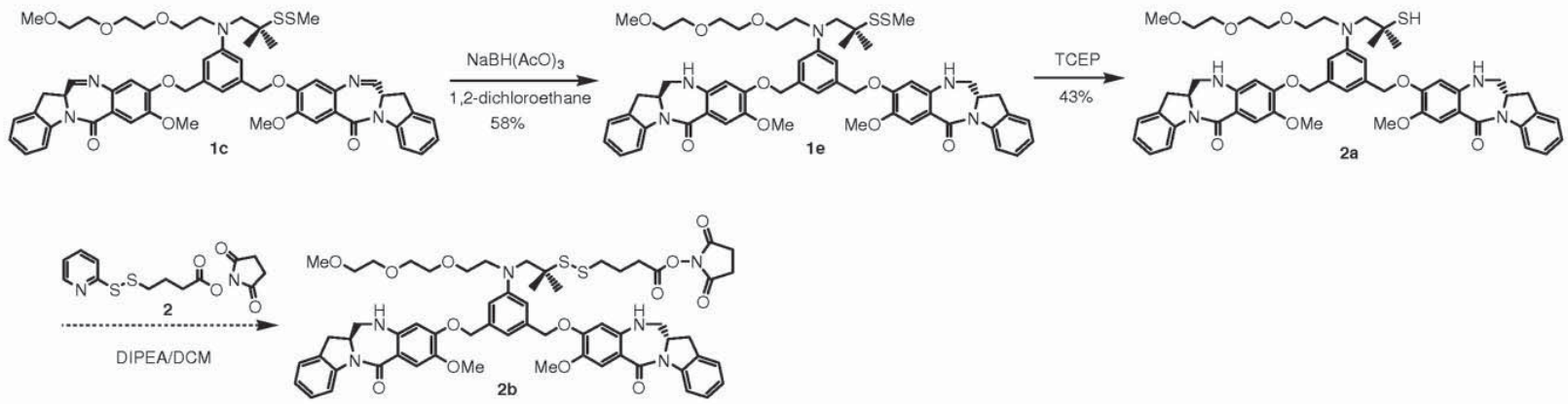


Figure 3. Synthetic Scheme of Dimers **3e-g**

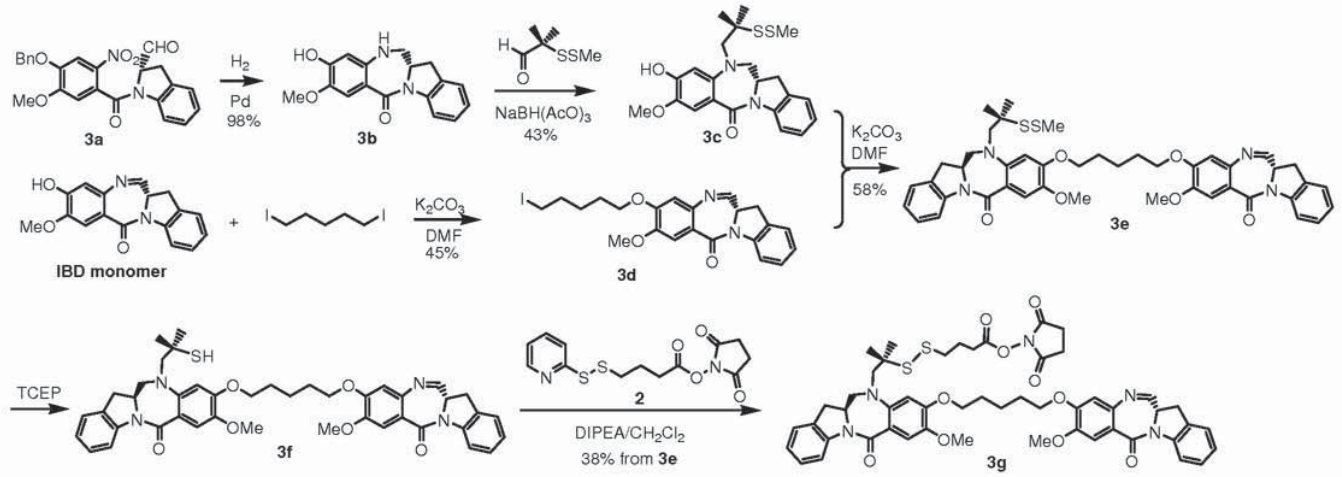


Figure 4. Synthetic Scheme of Dimers **4b-e**

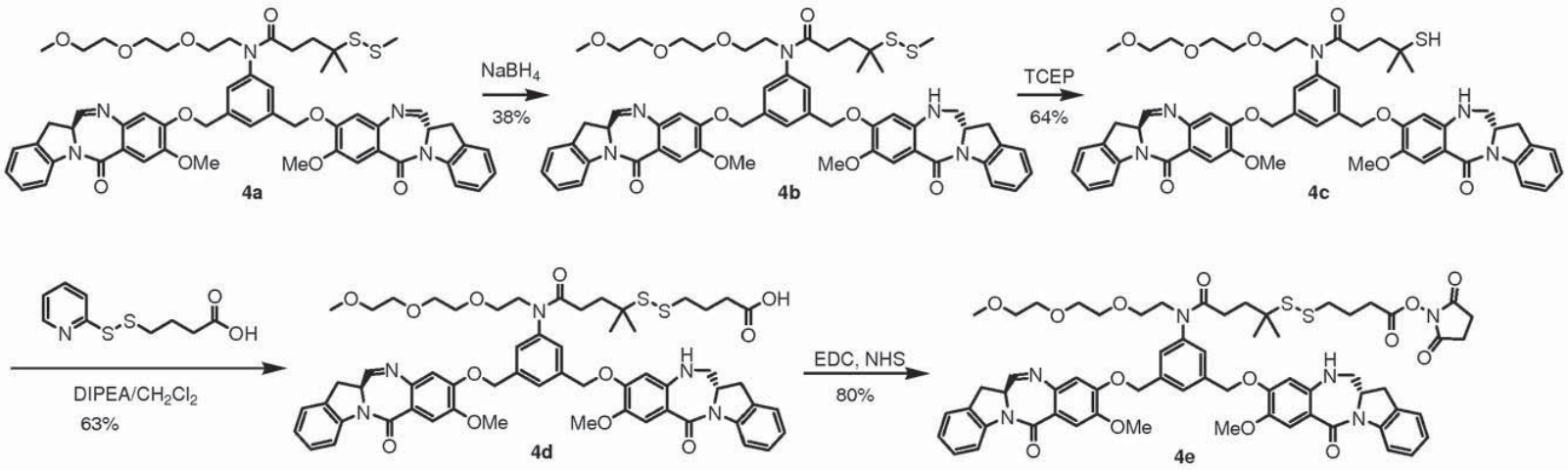


Figure 5. Synthetic Scheme of Linker **5e** and Dimers **5g-j**

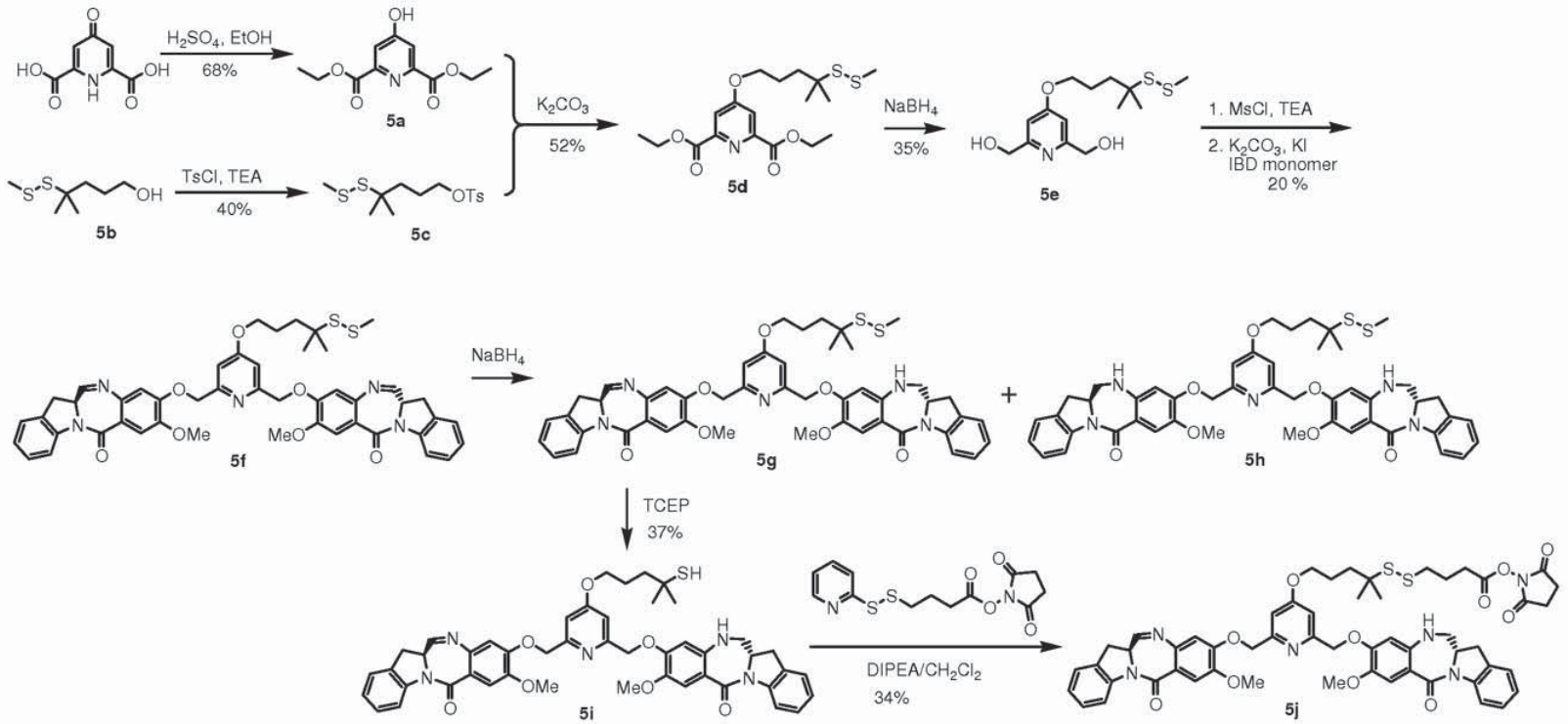


Figure 6. Synthetic Scheme of Linker **6a** and Dimers **6c-d**

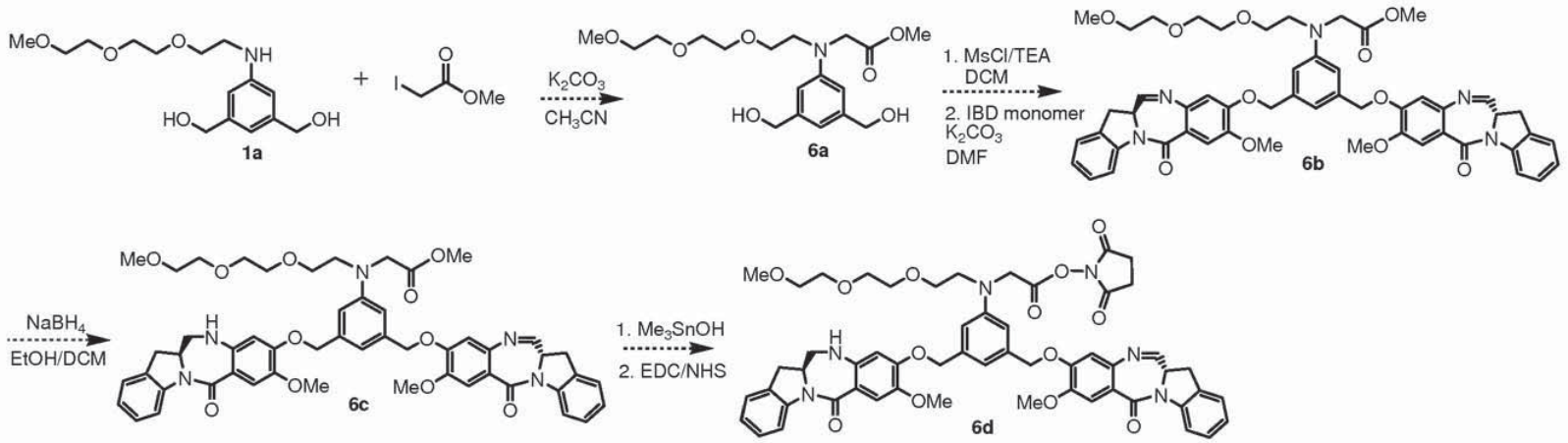


Figure 7. Synthetic Scheme of PEG Modified Linkers **7b** and Dimers **7d-f**

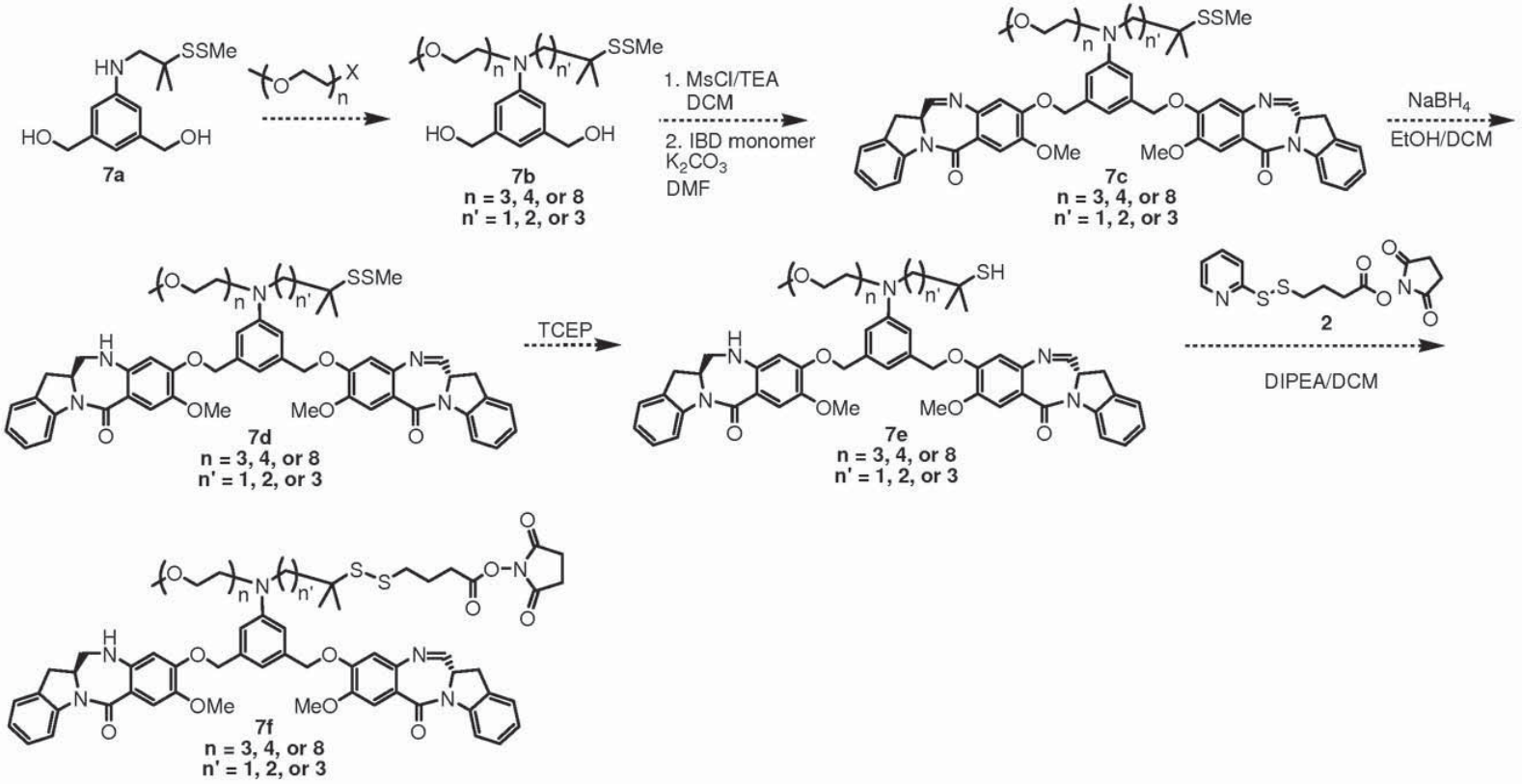


Figure 8. Synthetic Scheme of Thiol-containing Dimers **8b-e**

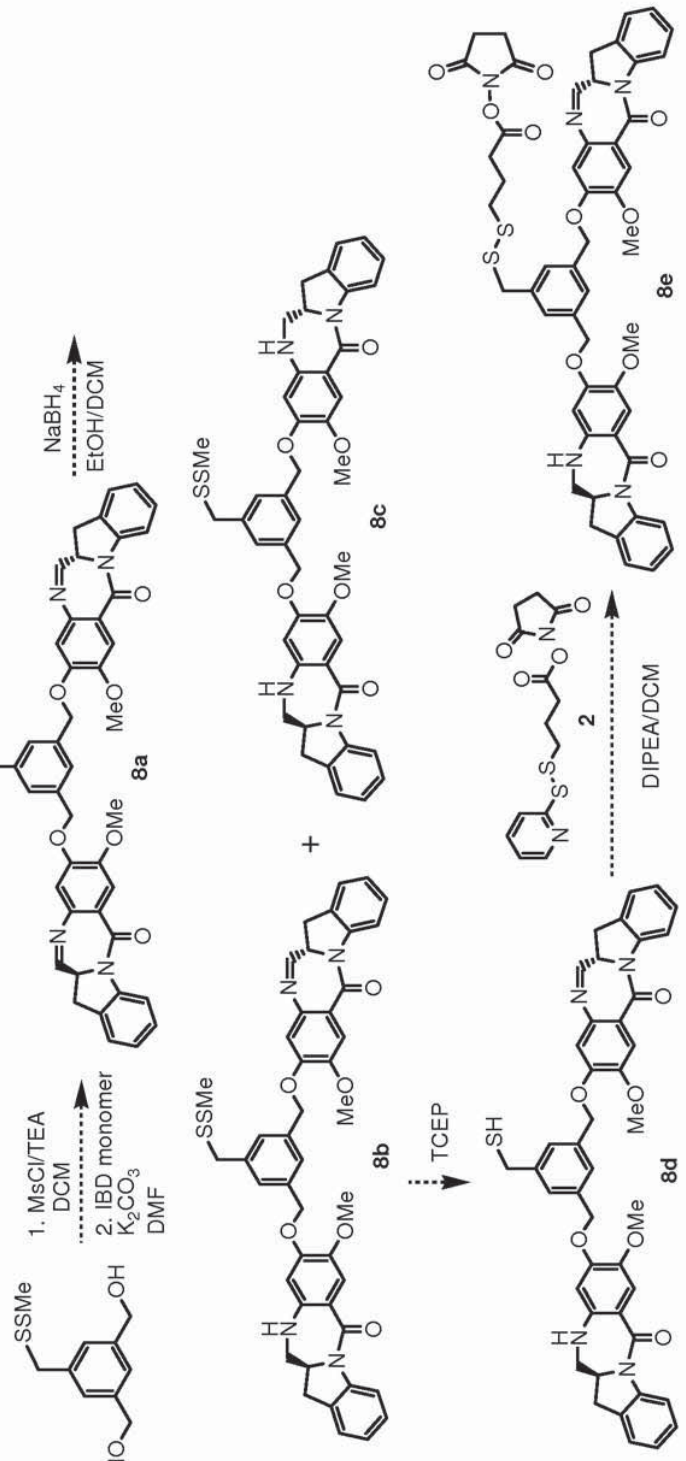


Figure 9. Synthetic Scheme of Dimers **17d-g** Containing a Tertiary Amine

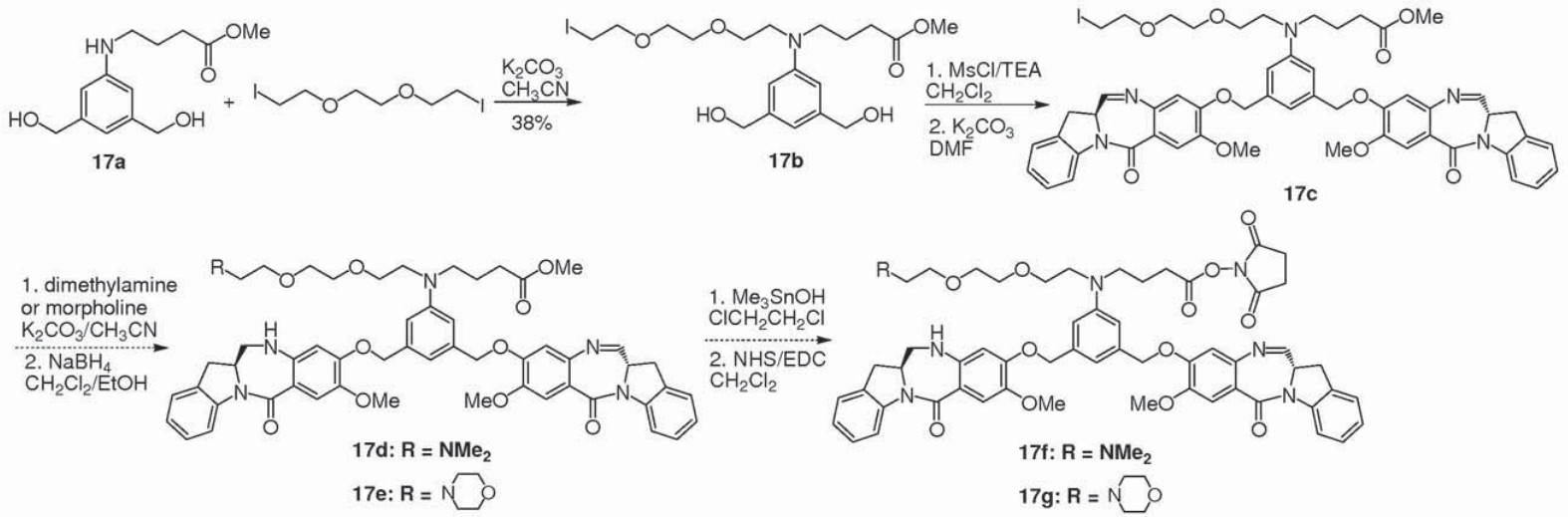


Figure 10. Synthetic Scheme of Dimers **18c-f** Containing a Tertiary Amine

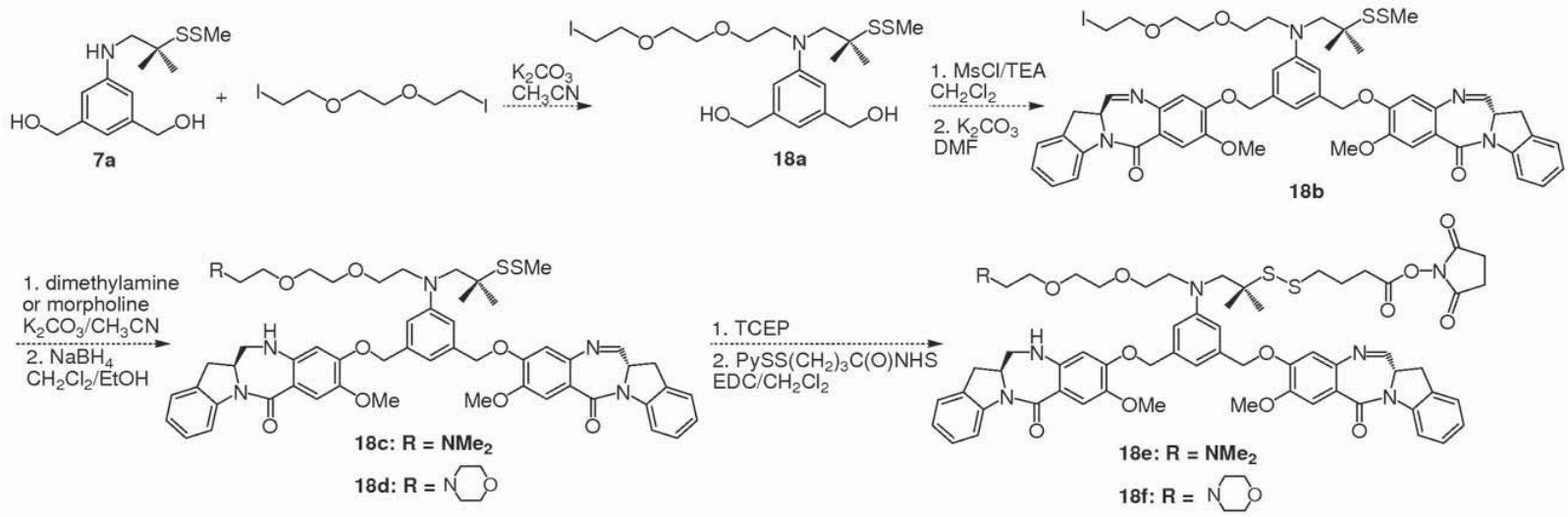


Figure 11. Synthetic Scheme of Dimers **21f-g** Containing a Peptide Linker

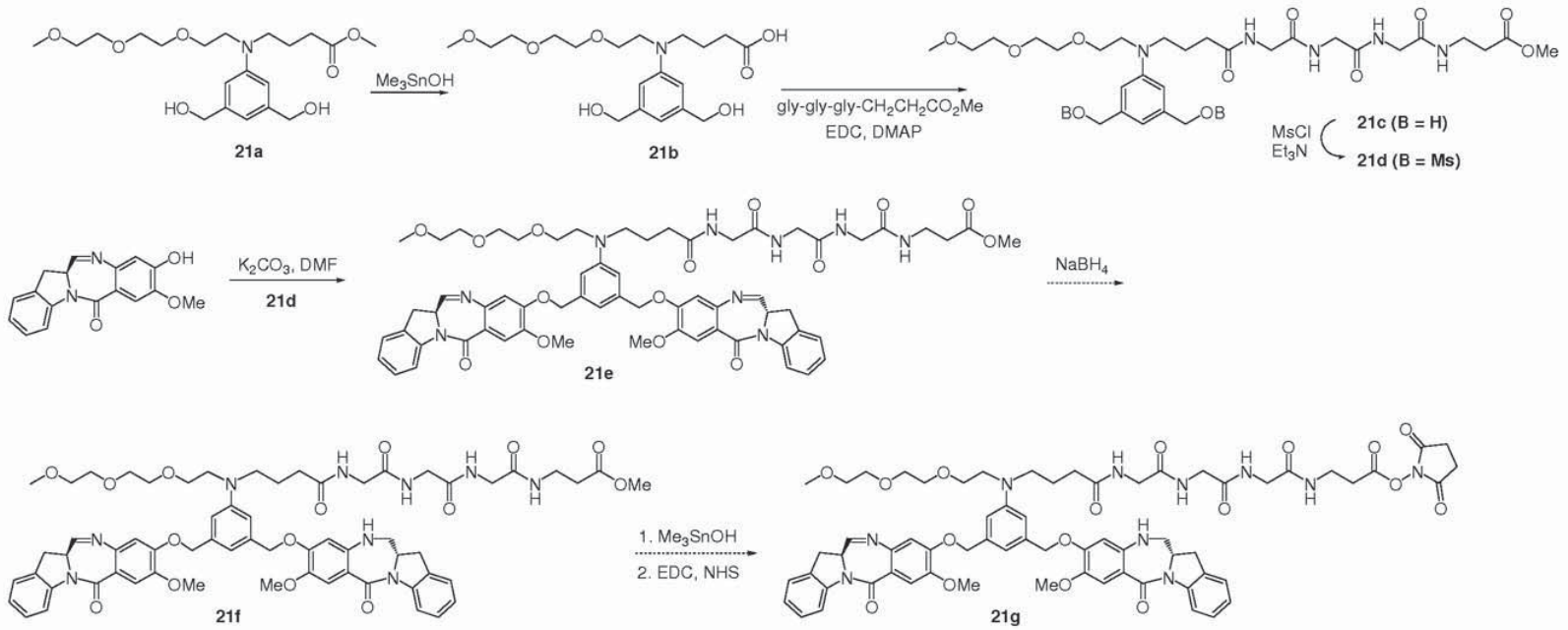


Figure 12A. Synthetic Scheme of the One-step Thioacetyl Linkable Dimers **9a-b**

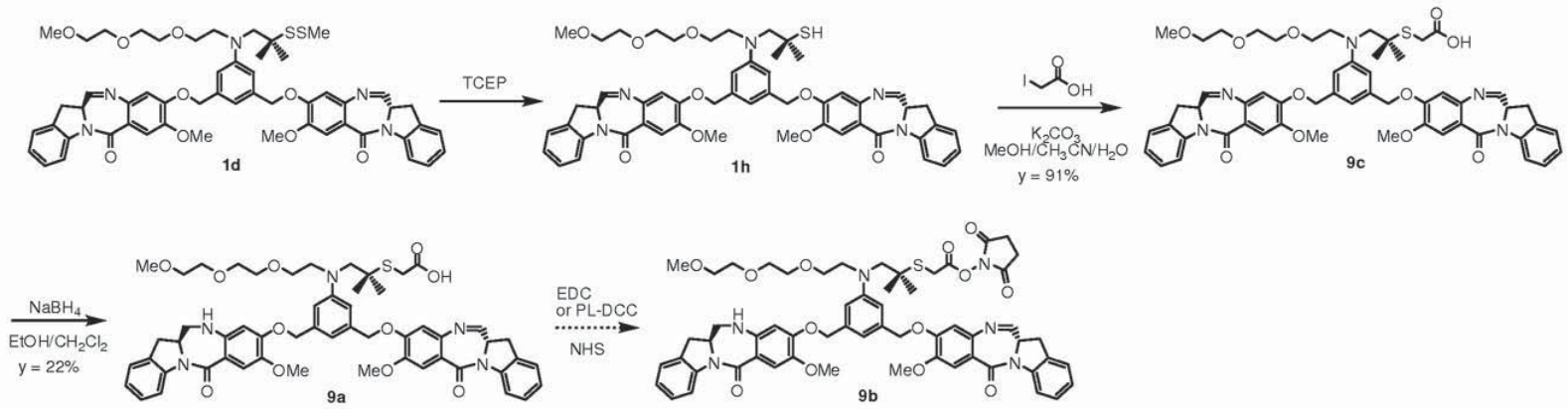


Figure 12B. Alternative Synthetic Scheme of the One-step Thioacetyl Linkable Dimers **9a-b**

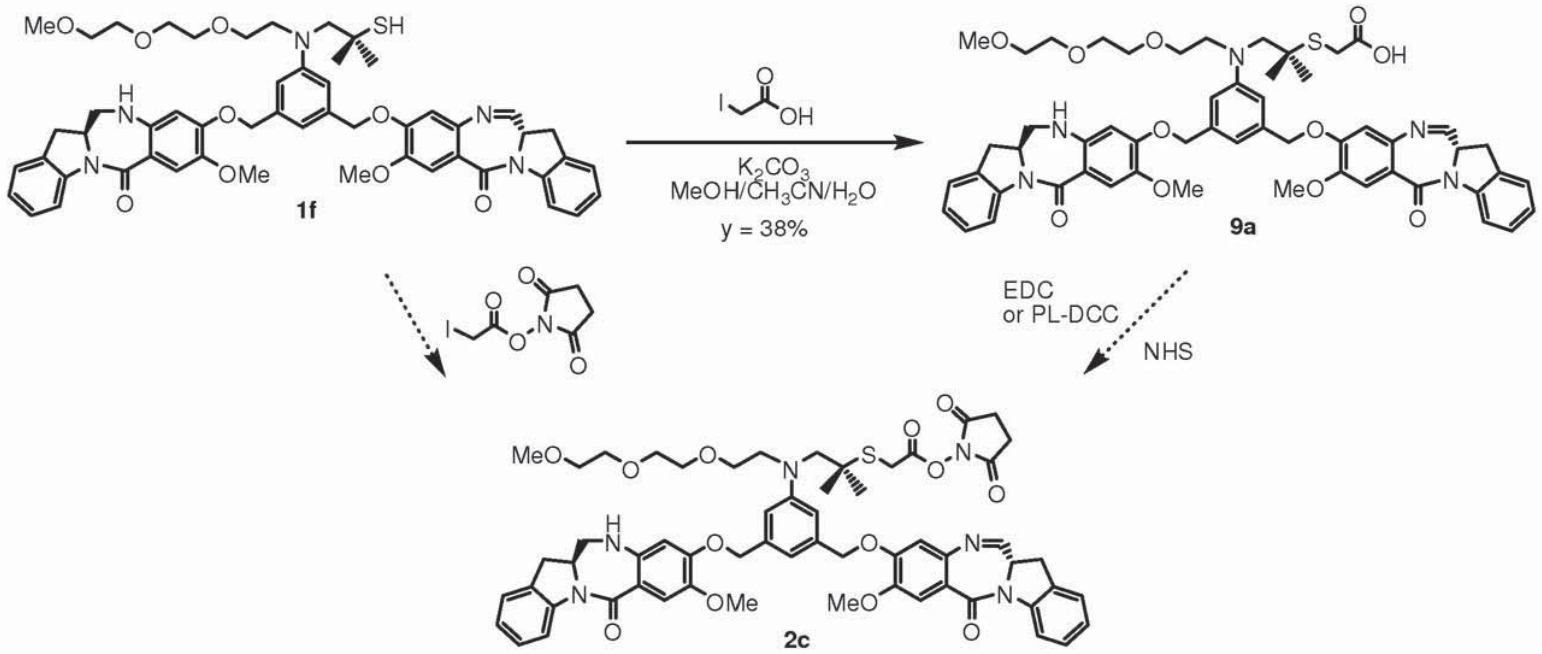


Figure 13. Synthetic Scheme of the One-step BMPS Linkable Dimer **10**

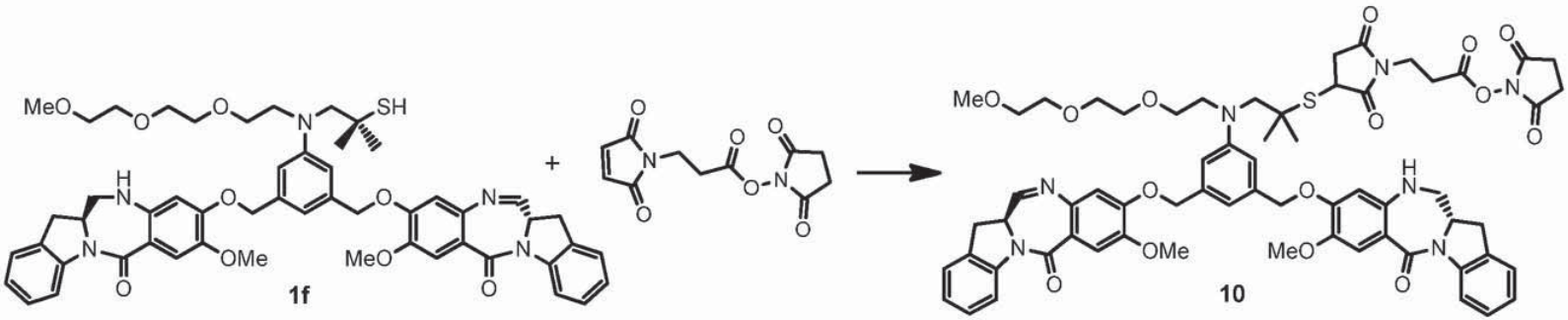


Figure 14. Synthetic Scheme of the One-step SMCC Linkable Dimer **11**

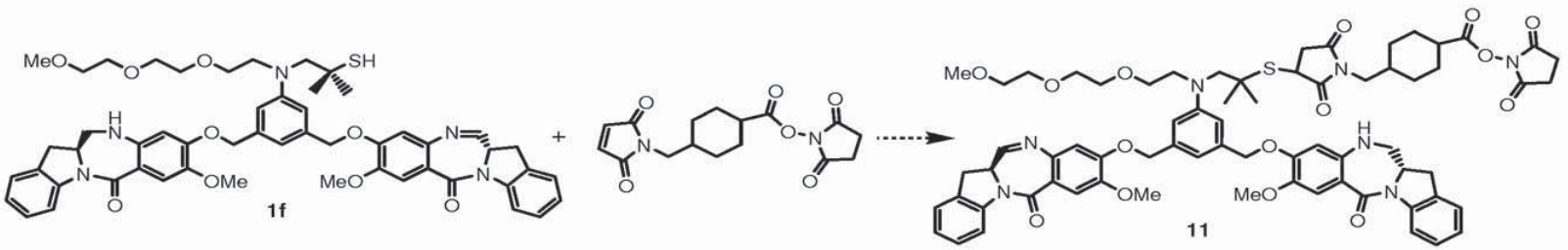


Figure 15. Synthetic Scheme of the One-step Sulfo-SPDB Linkable Dimer **12**

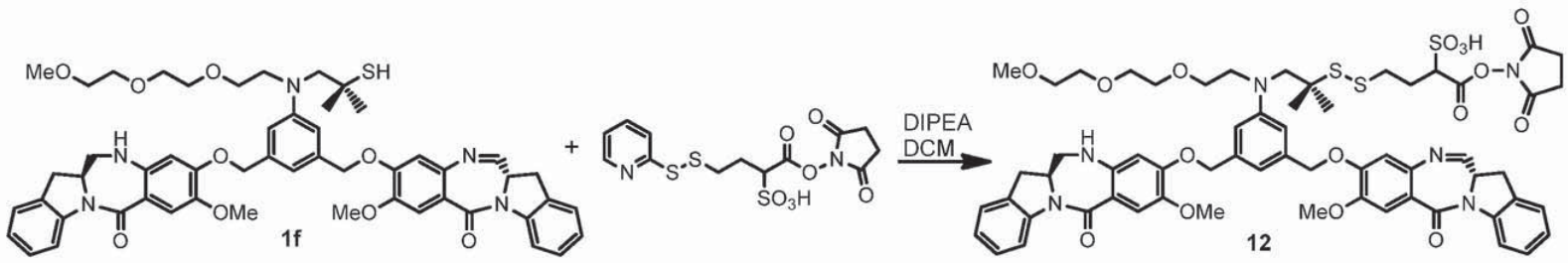


Figure 16. Synthetic Scheme of the One-step SPP Linkable Dimer **13**

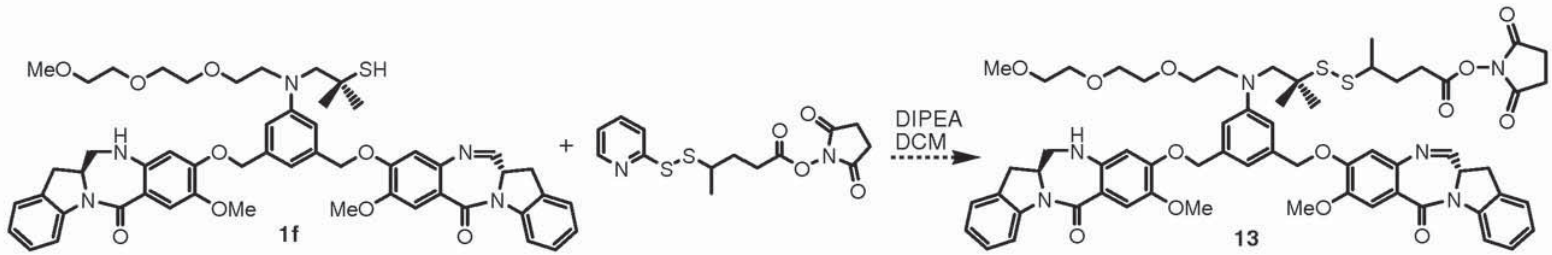


Figure 17. Synthetic Scheme of the One-step Thioacetyl Linkable Dimers **14a-b**

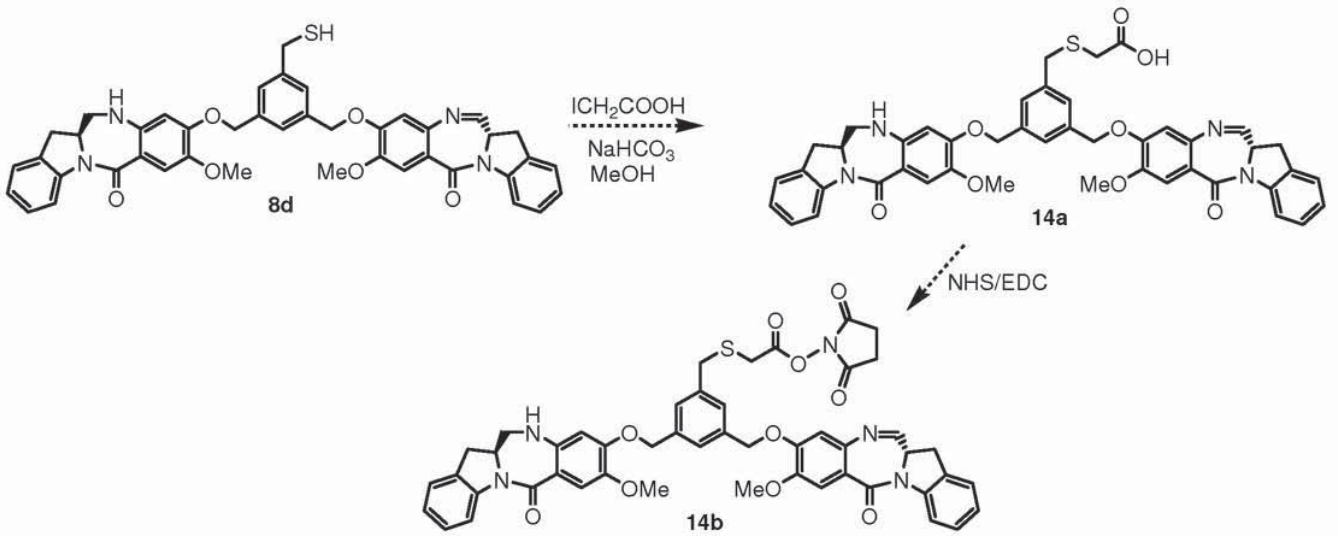
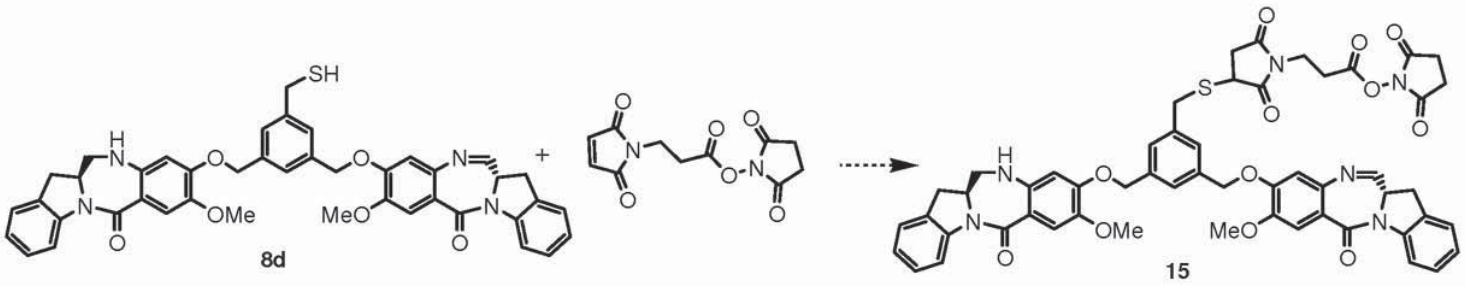


Figure 18. Synthetic Scheme of the One-step BMPS Linkable Dimer **15**



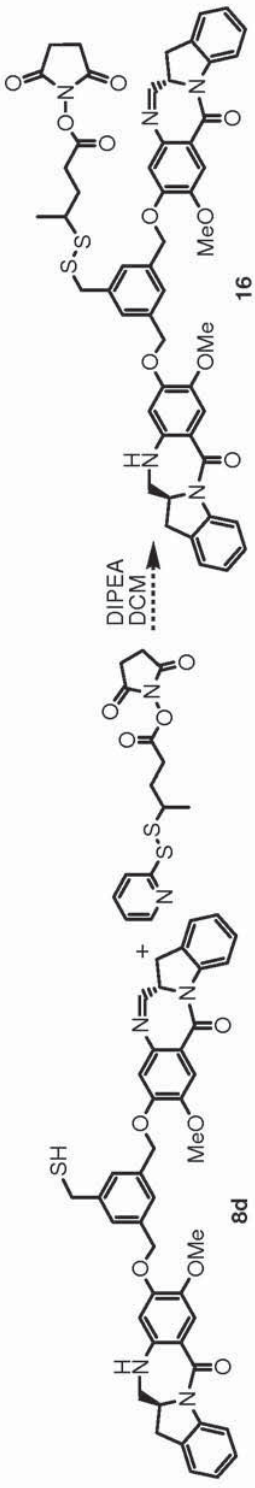


Figure 19. Synthetic Scheme of the One-step SPP Linkable Dimer **16**

Figure 20. Synthetic Scheme for a Two-step Mono-imine Dimer Synthesis

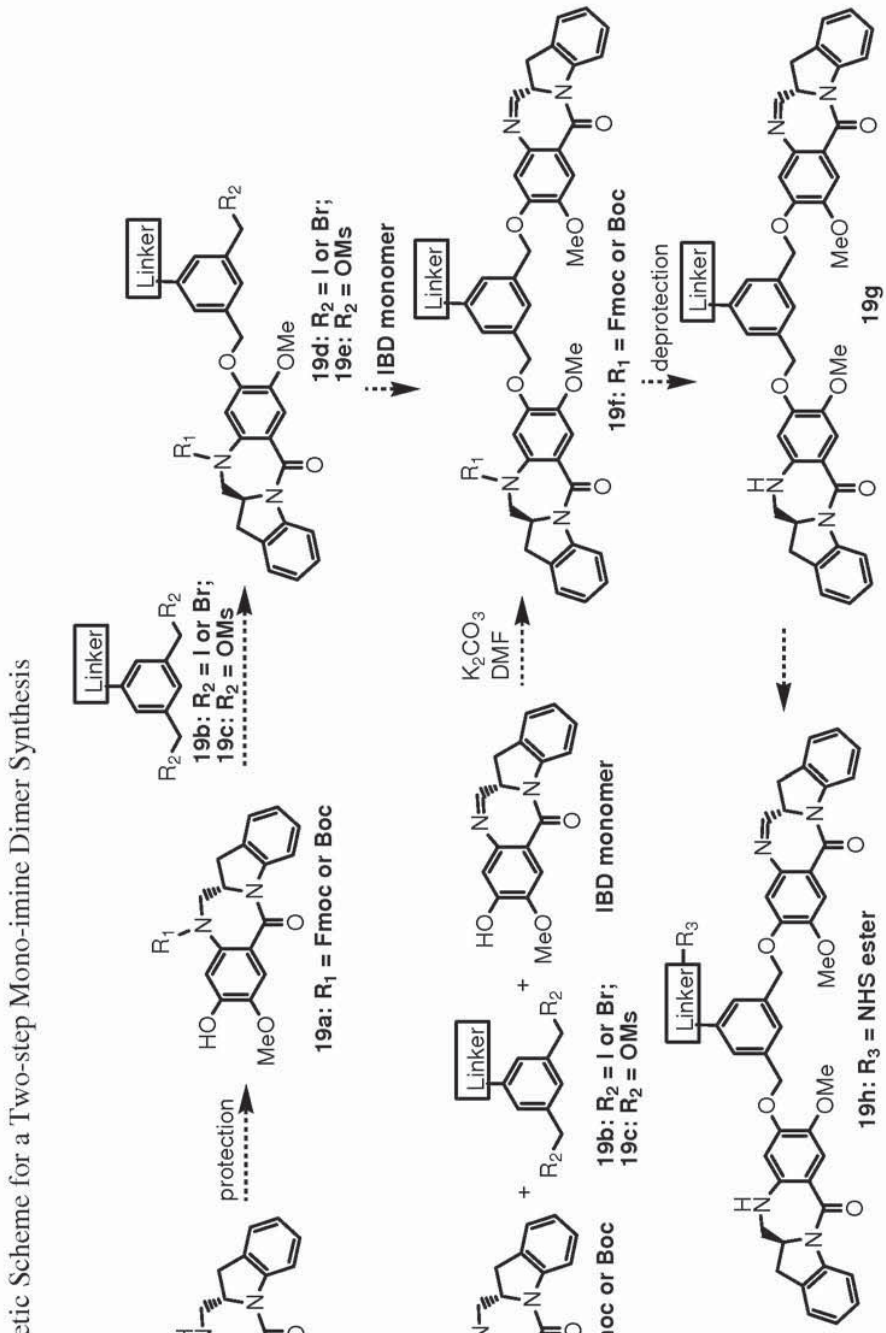


Figure 21. Synthetic Scheme for a Two-step Di-reduced Dimer Synthesis

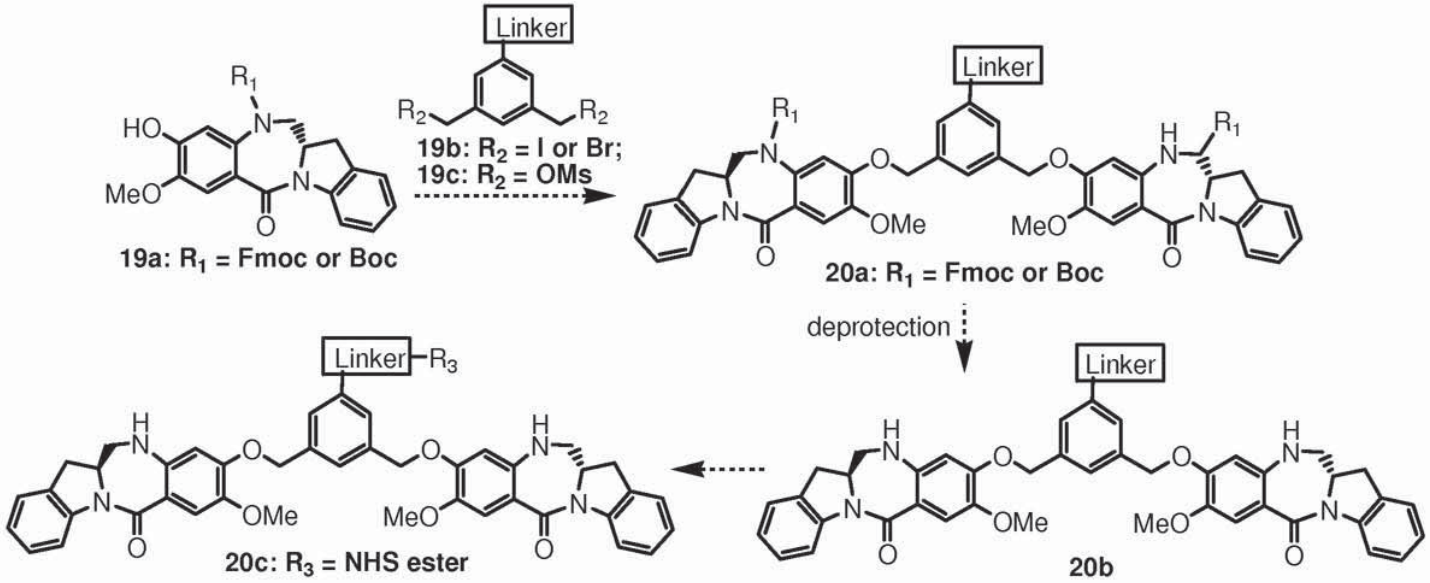


Figure 22. One Step Conjugation Scheme

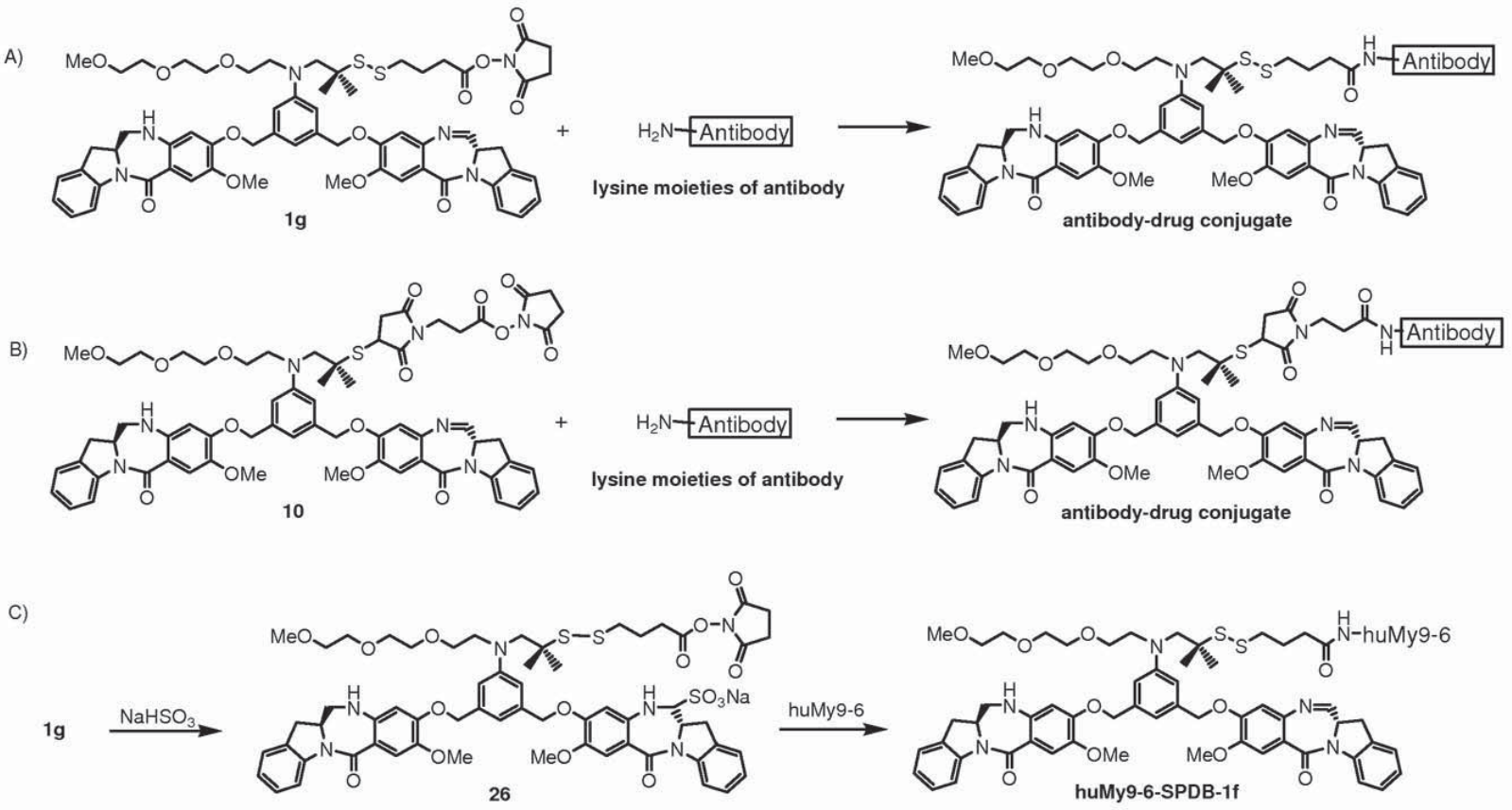


Figure 23. Two-step Conjugation Scheme

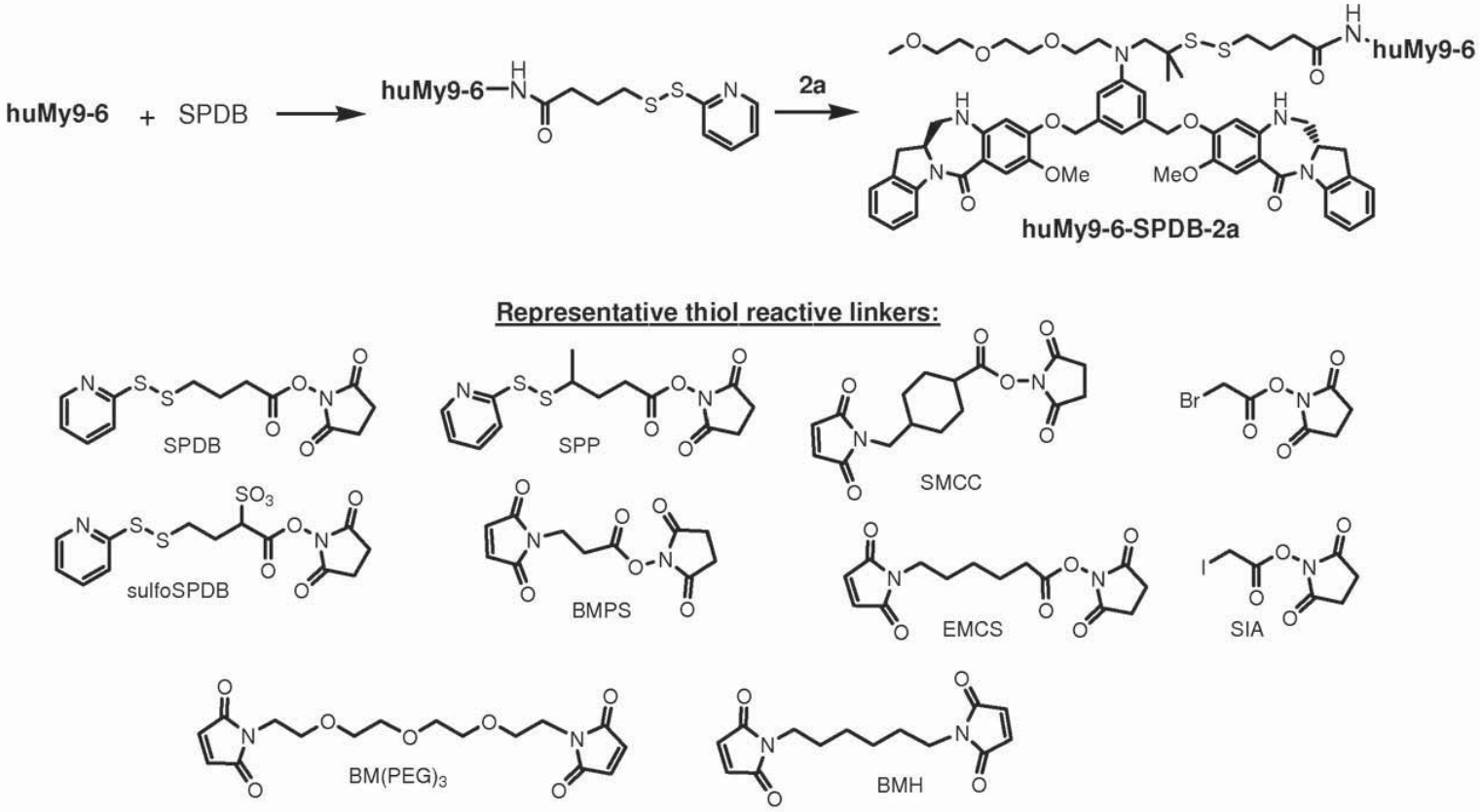
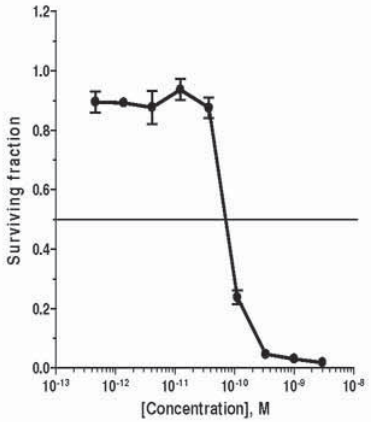
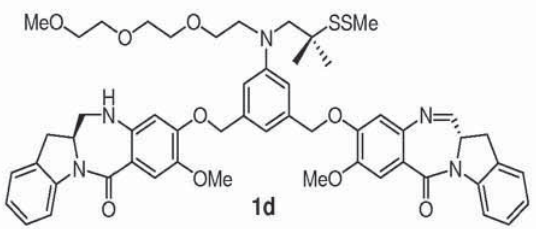


Figure 24. Antiproliferative Activity of Methyldithio Dimer **1d** against (A) Namalwa cells, (B) HL60/QC cells, and (C) KB cells

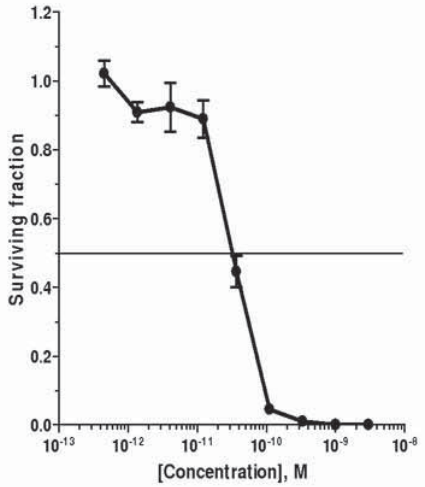
A)





1d

B)



C)

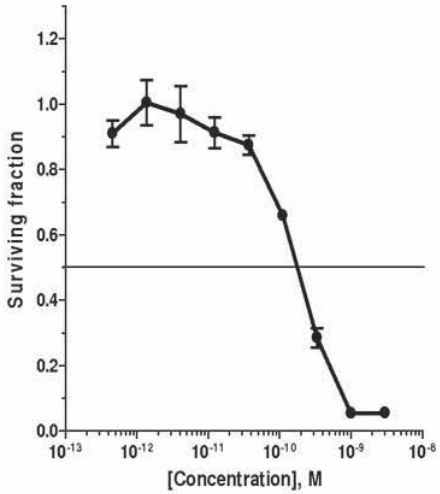


Figure 25. Antiproliferative Activity of huMY9-6-SPDB-**1f** against (A) HL60/QC (Ag^+) cells with and without blocking of antigen binding sites, (B) HL60/ATCC (Ag^+) cells, and (C) NB-4 (Ag^+) cells

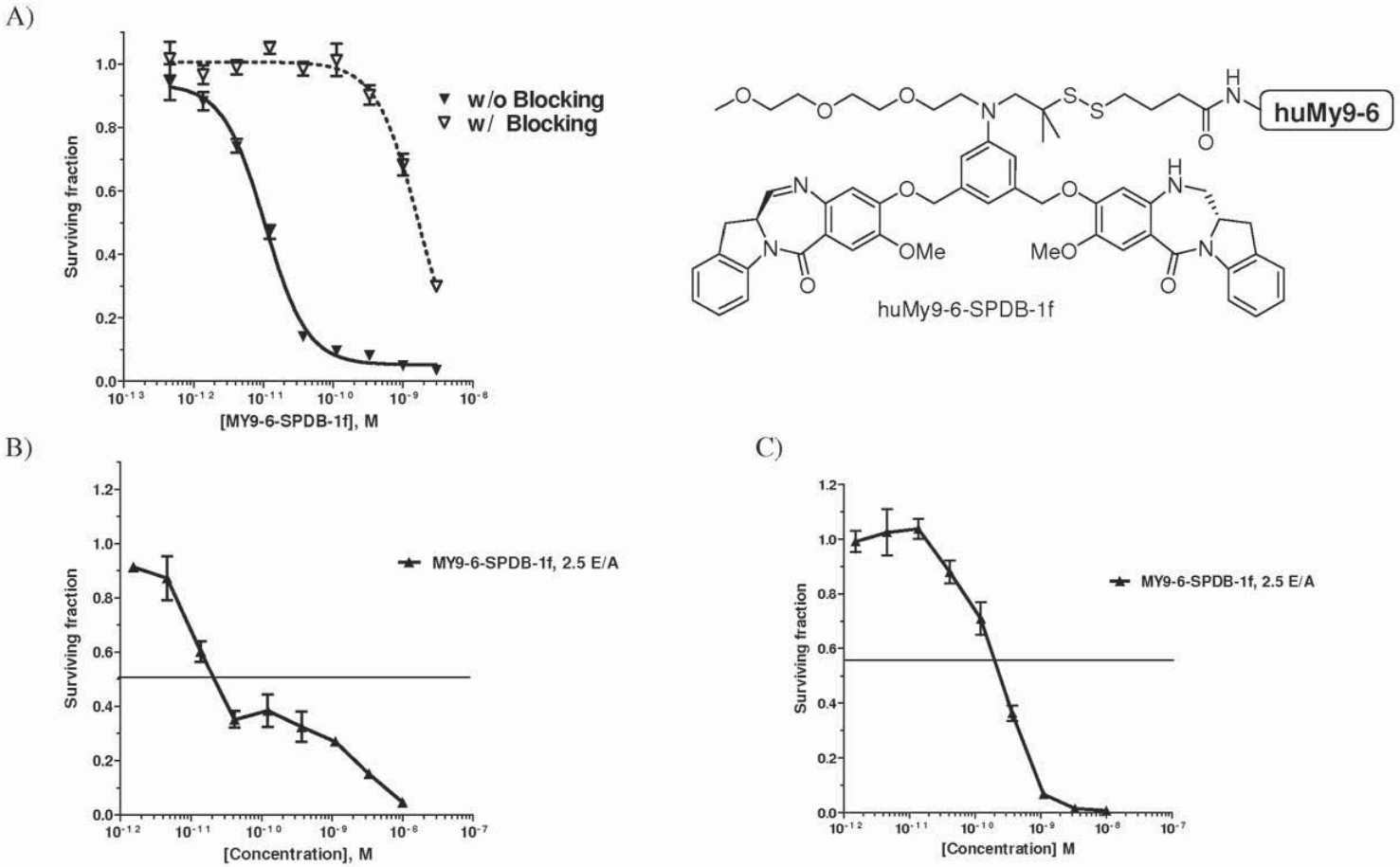
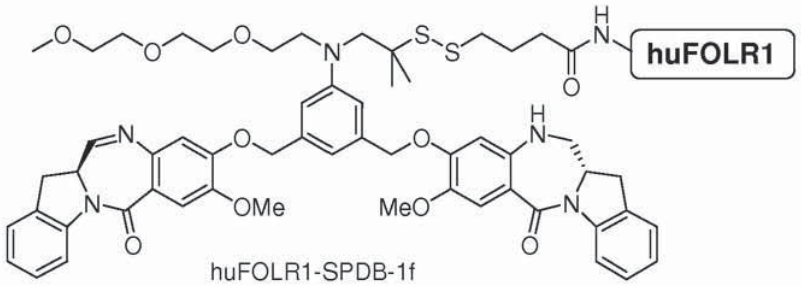


Figure 26. Antiproliferative Activity of huFOLR1-SPDB-**1f** against KB (Ag^+) cells with and without blocking of antigen binding sites



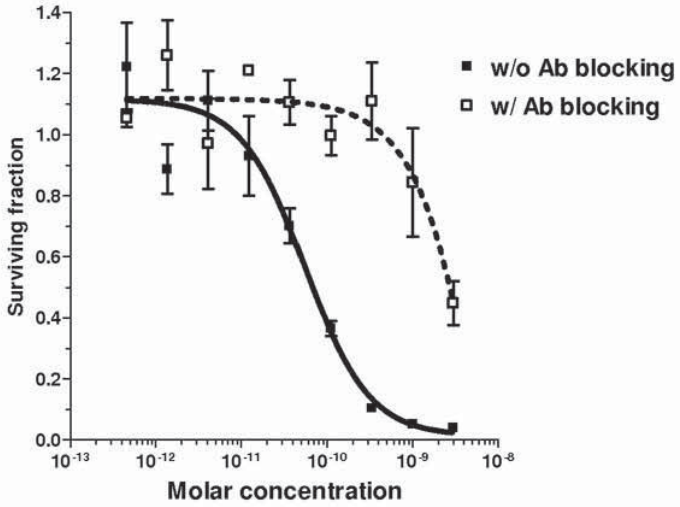
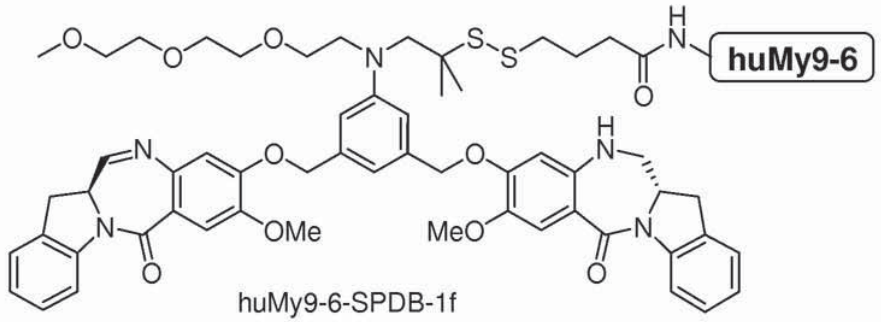


Figure 27. Binding Affinity of huMY9-6-SPDB-**1f** (FACS analysis)



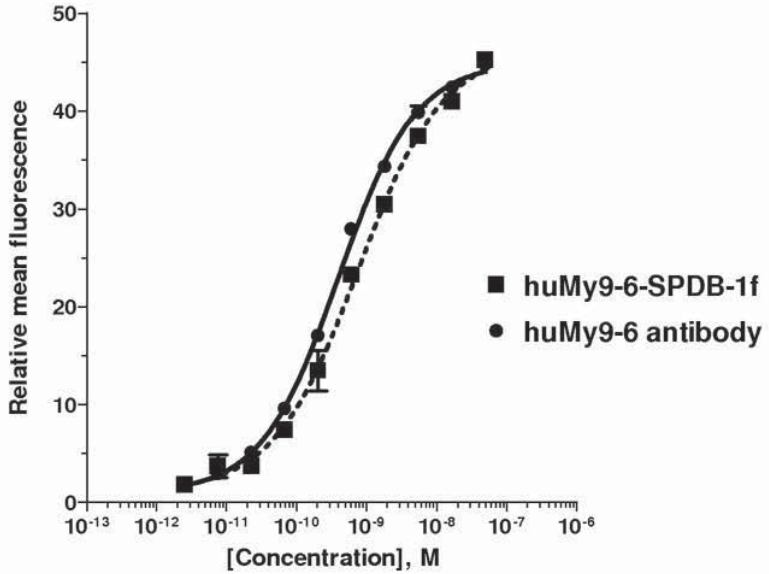


Figure 28. *In vivo* Efficacy of huMy9-6-SPDB-**1f** in HL60/QC Tumor Bearing Nude Mice

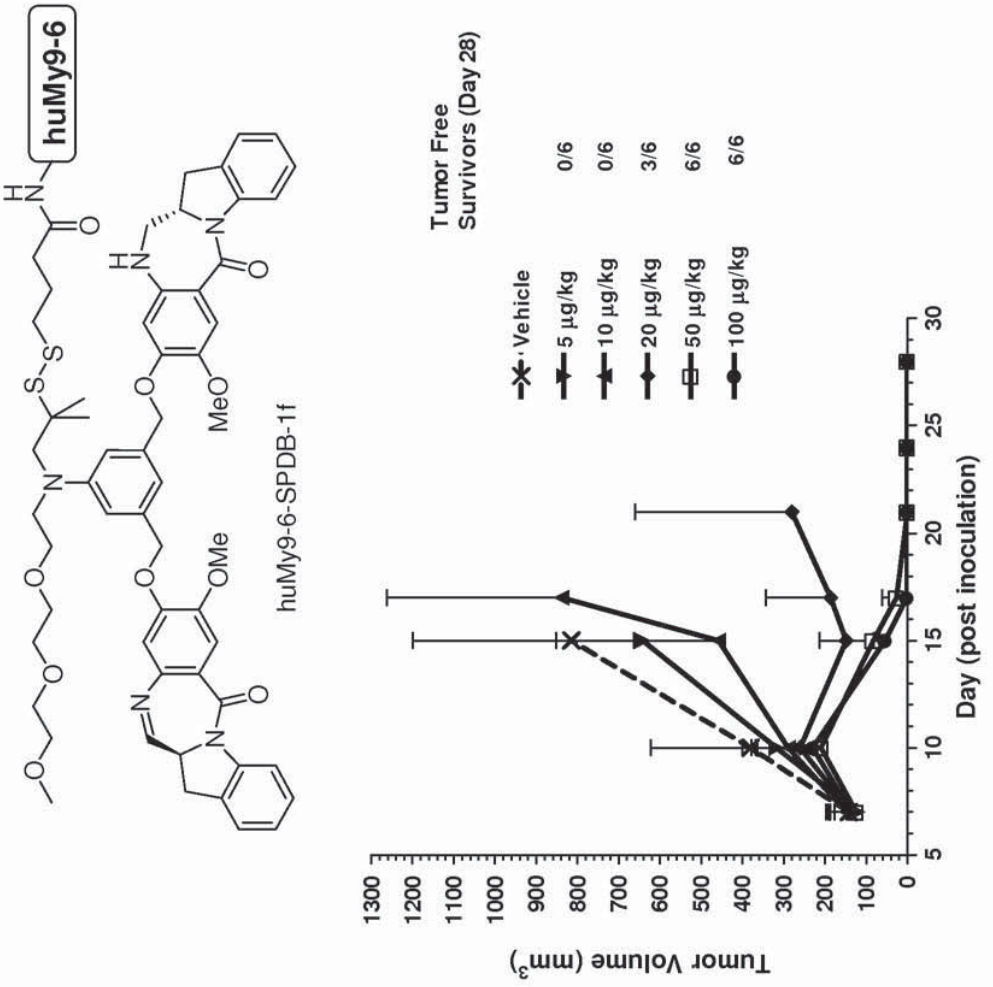


Figure 29. Antiproliferative Activity of huMY9-6-SPDB-**1f** against Antigen Positive Cell Line (A) HL60/QC cells, (B) HL60/ATCC cells, (C) NB-4 cells, and HEL 92.1.7 cells (D)

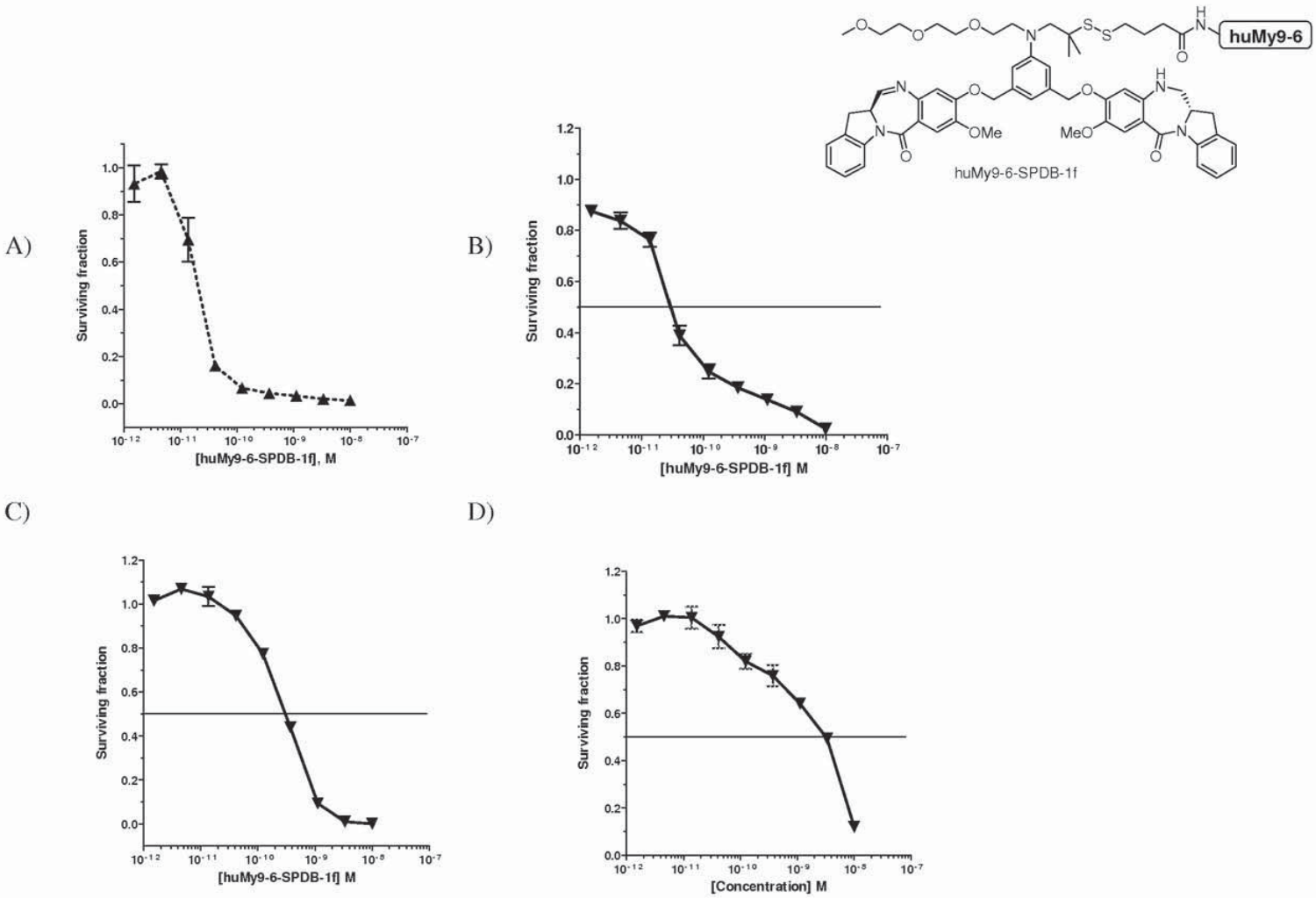


Figure 30. Synthetic Scheme for Thioether-containing Linker Disulfides **27e-h**.

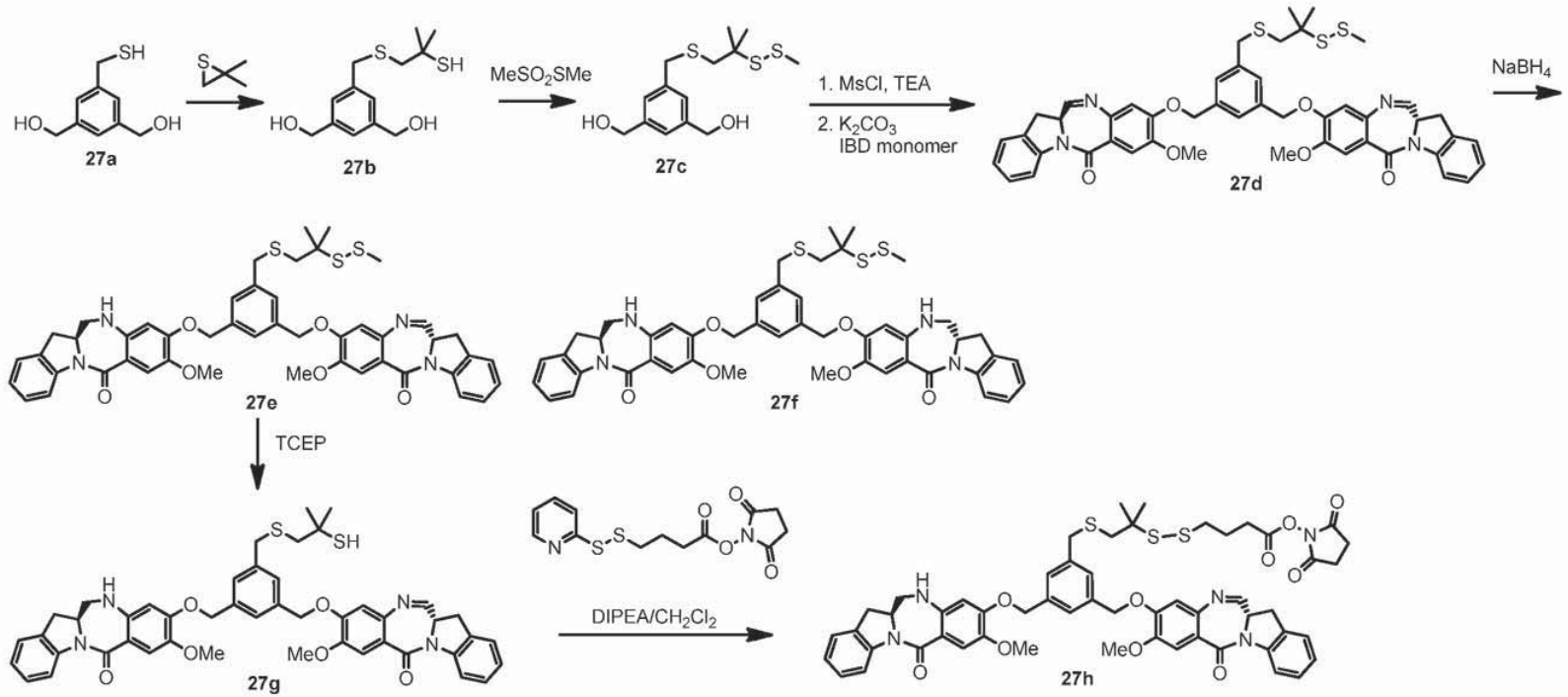


Figure 31. Synthetic Scheme of Dimers **28c-f**

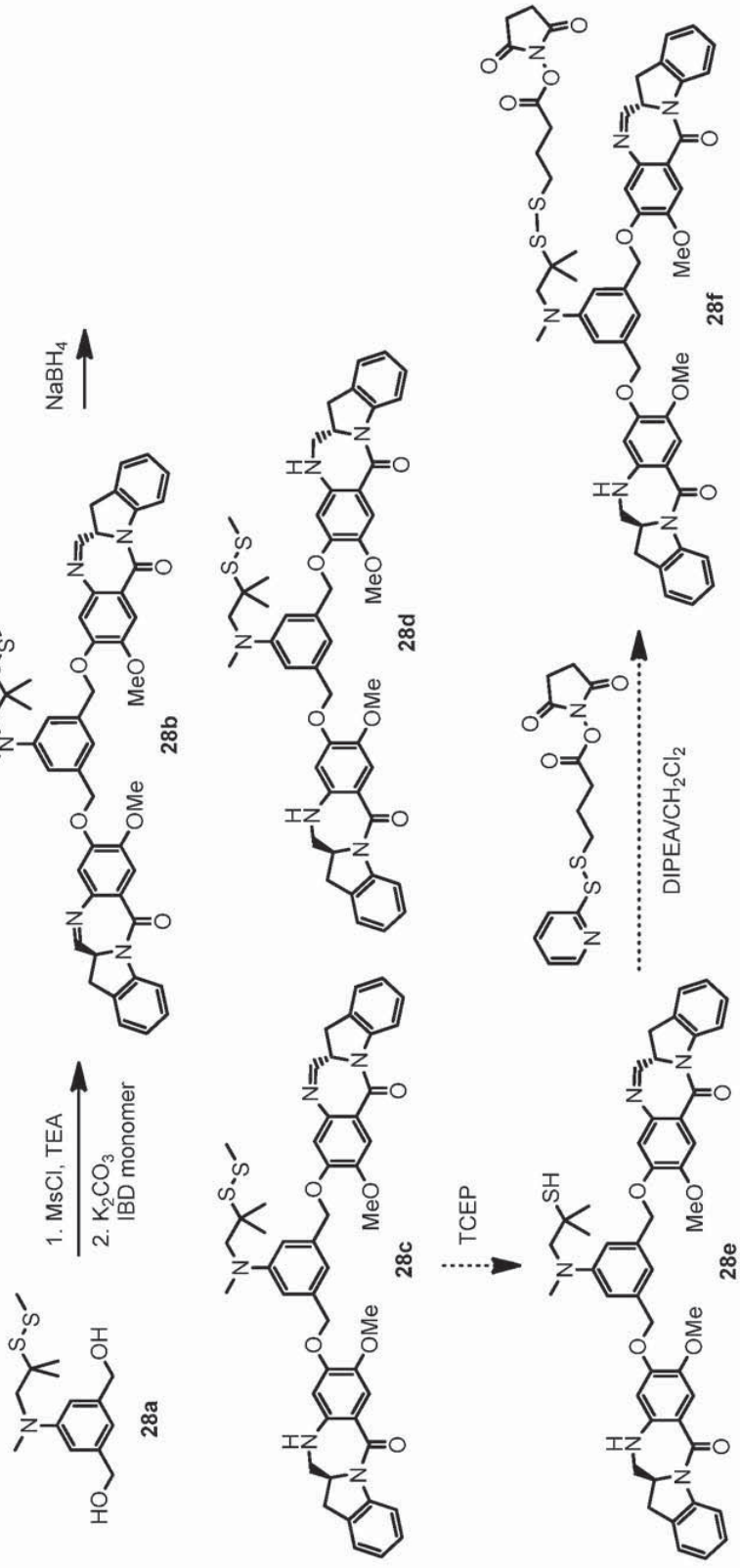


Figure 32. Synthetic Scheme for Phenyl Linked Dimers **29b-c**

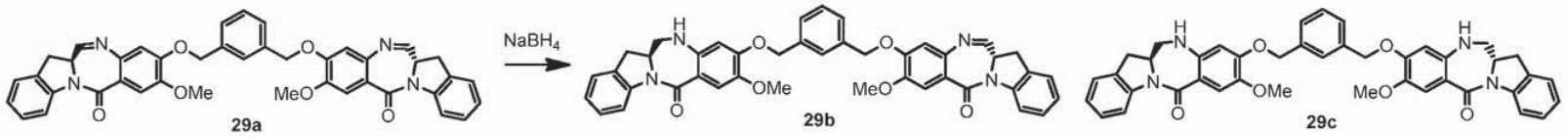


Figure 33. Alternate Two-step Mono-imine Dimer Synthesis

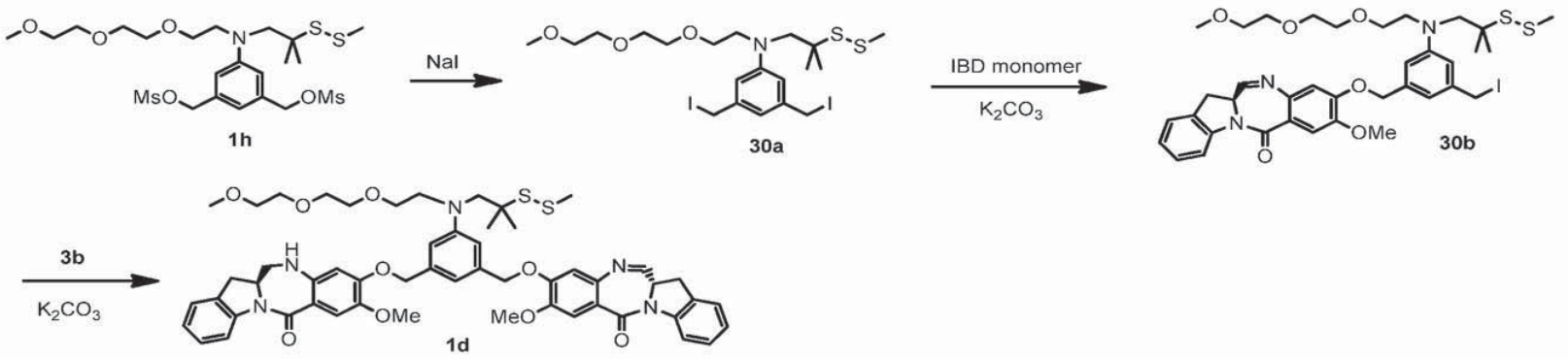


Figure 34. Antiproliferative Activity Comparing (A) huMy9-6-SPDB-**1f** and (B) huMy9-6-sulfoSPDB-**1f**, and (C) huMy9-6-BMPS-**1f** against HL60/QC (Ag^+) Cells with and without Blocking of Antigen Binding Sites

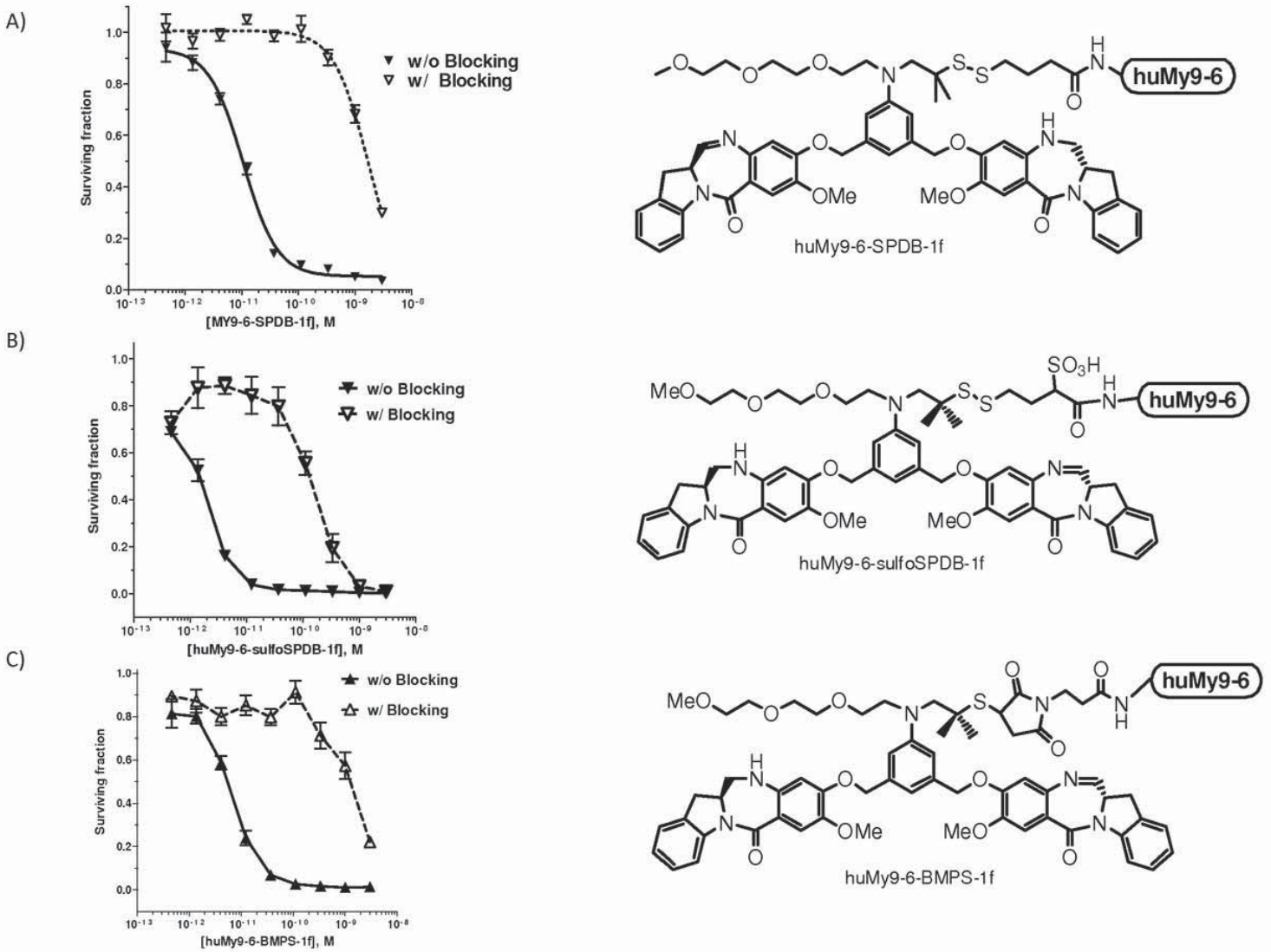
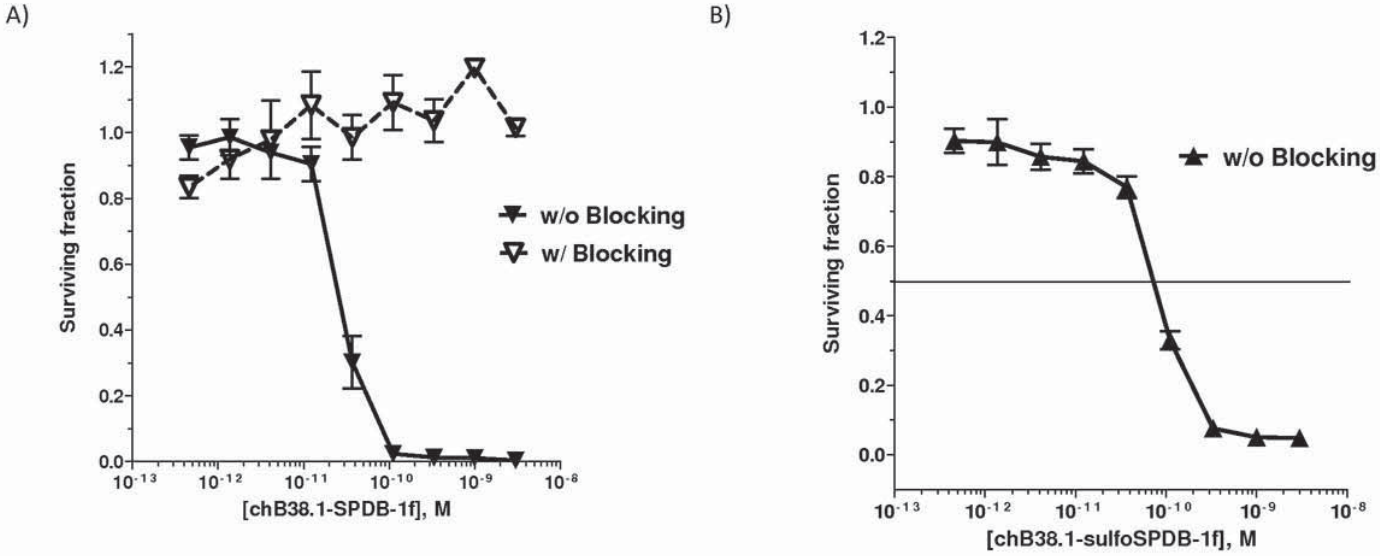


Figure 35. Antiproliferative Activity Comparing (A) chB38.1-SPDB-**1f** and (B) chB38.1-sulfoSPDB-**1f** against COLO205 (Ag^+) cells



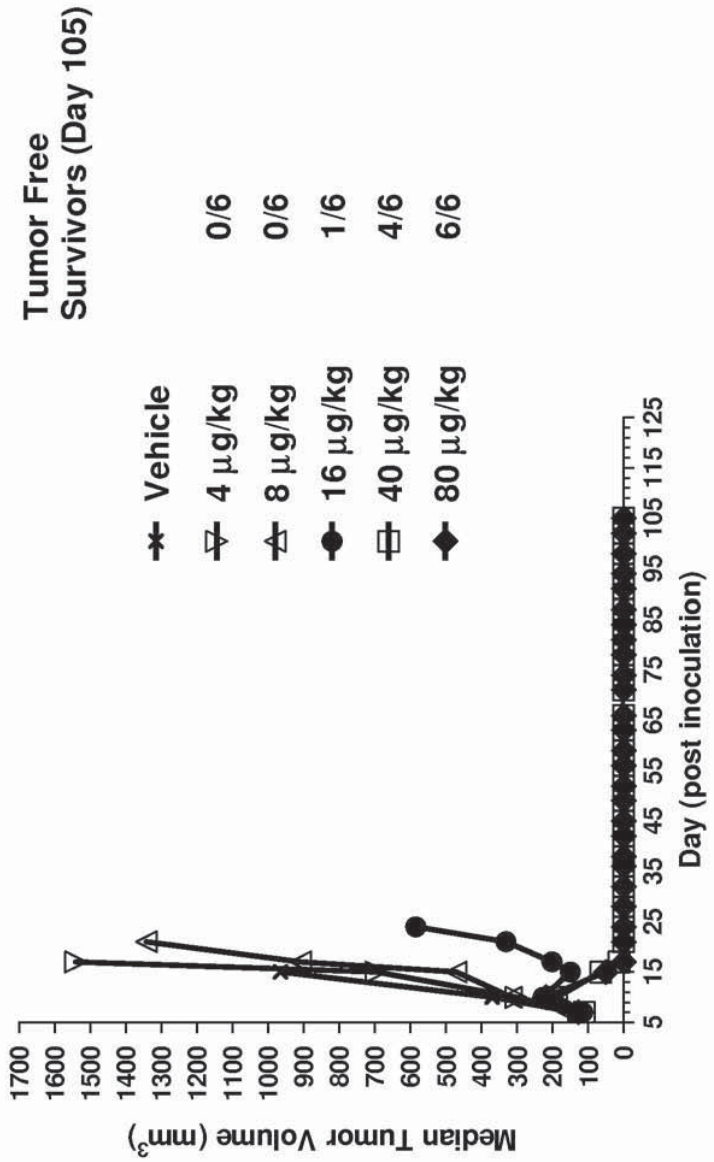


Figure 36. *In vivo* Efficacy of huMy9-6-SPDB-**1f** in HL60/QC Tumor Bearing Mice

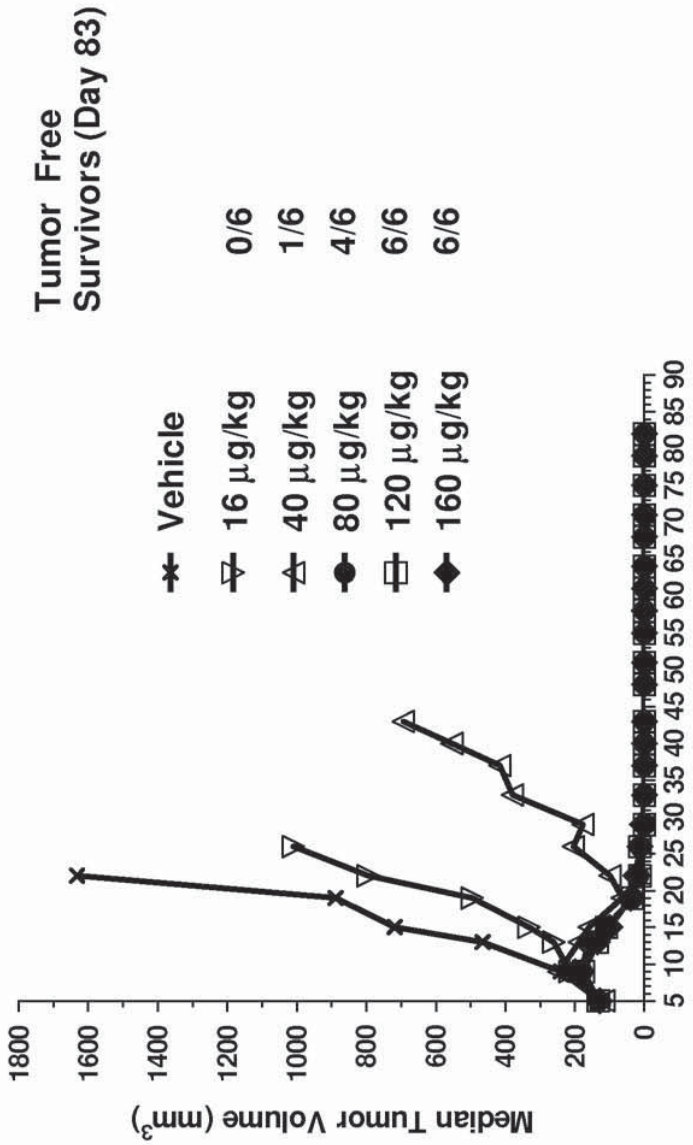


Figure 37. *In vivo* Efficacy of huFOLR1-SPDB-**1f** in KB Tumor Bearing Mice

Figure 38. Synthetic Scheme of Compound **1**

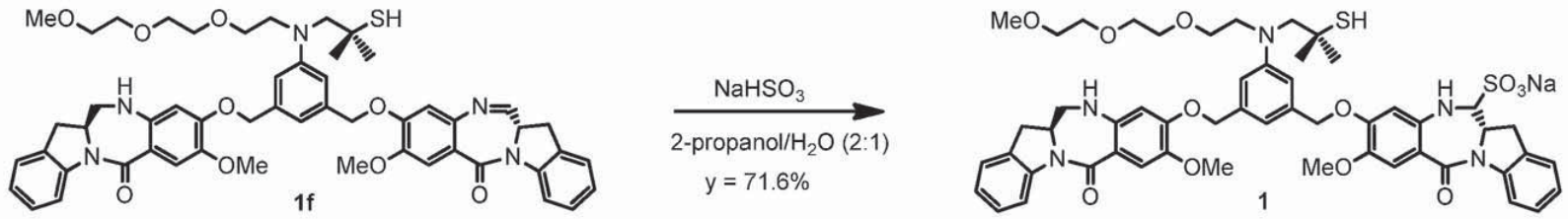


Figure 39. Synthetic Scheme of Compound **1d** with 5-ethyl-2-methylpyridine borane (PEMB)

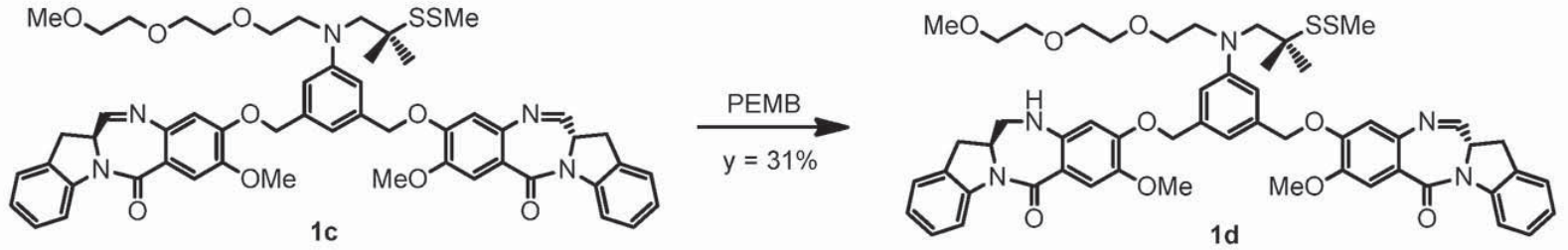


Figure 40. Synthetic Scheme of Compound **1d** with sodium triacetoxyborohydride (STAB)

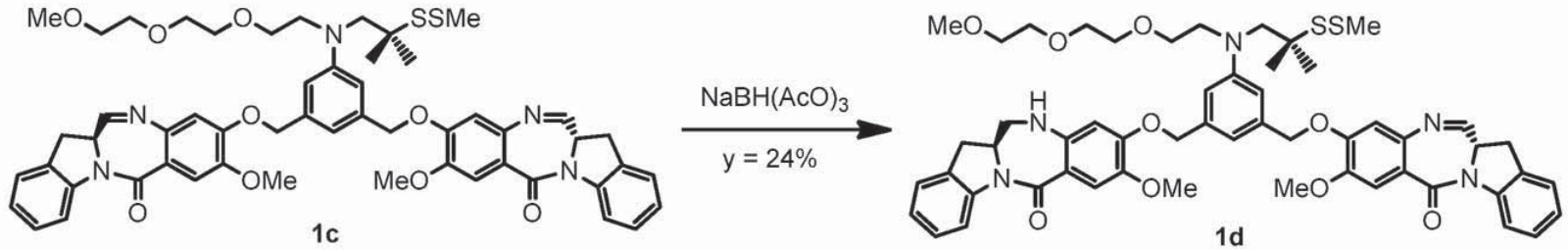


Figure 41. Synthetic Scheme of Compound **31a-c.**

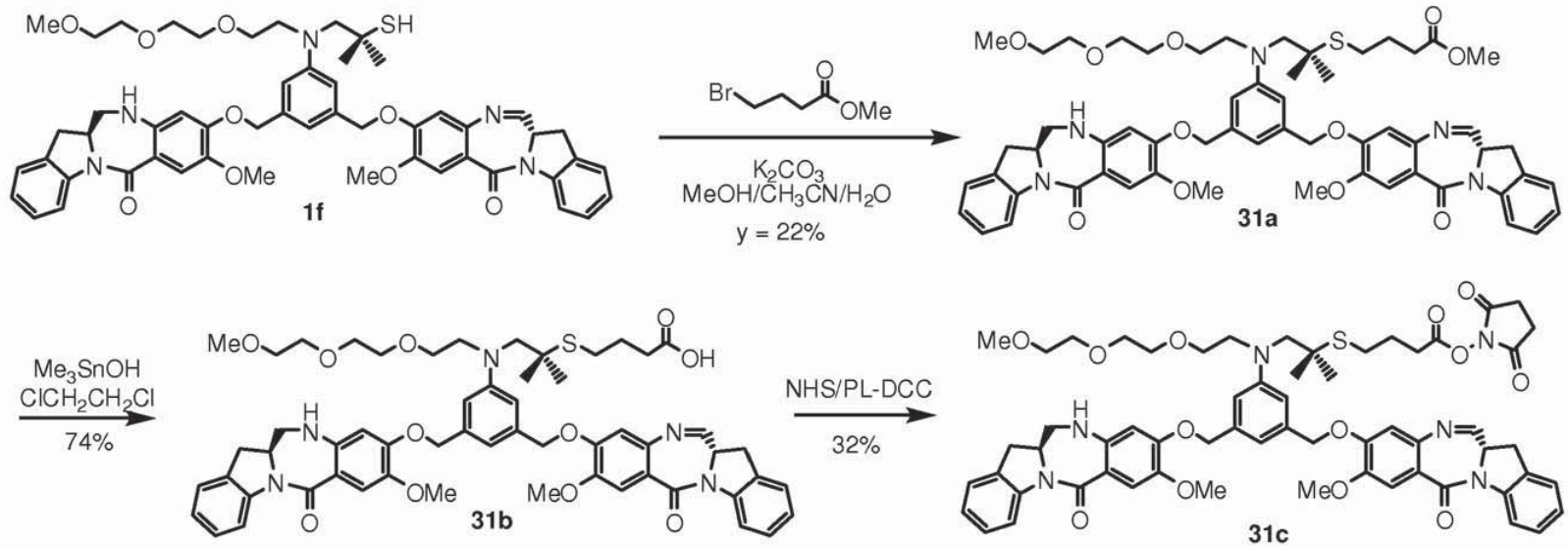
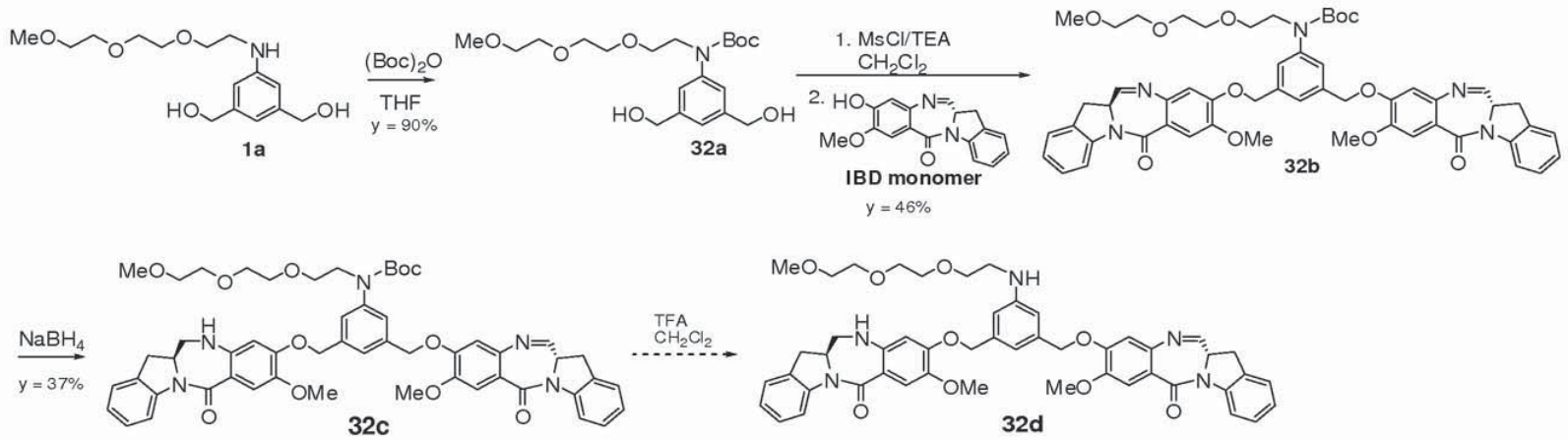


Figure 42. Synthetic Scheme of Compound **32d**



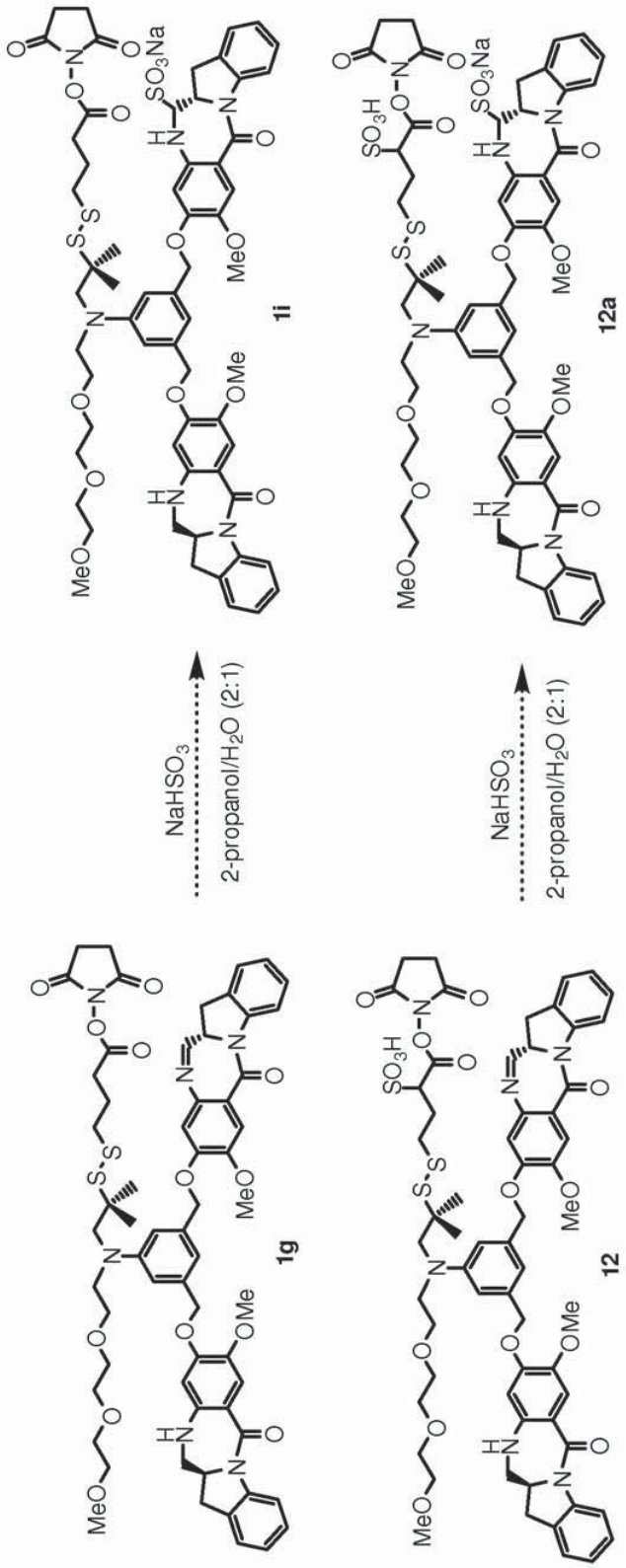
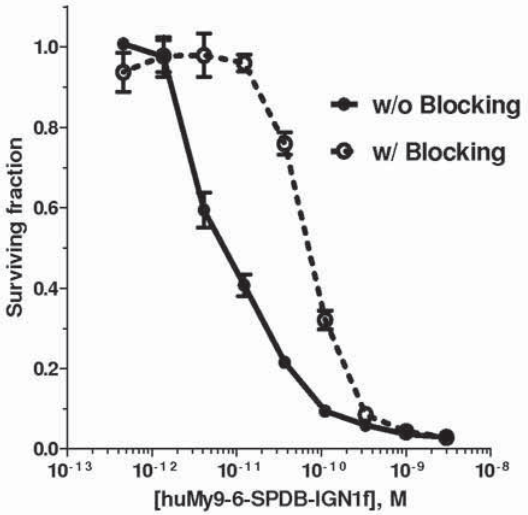
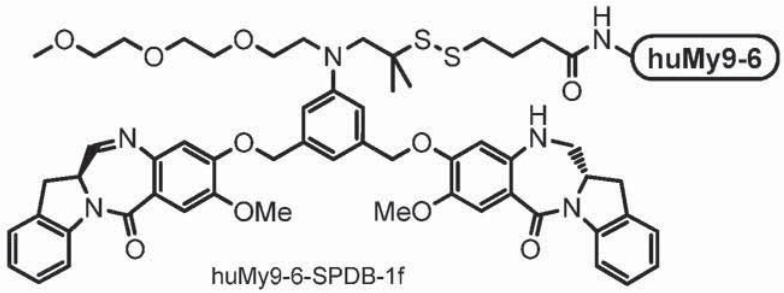


Figure 43. Synthetic Scheme of Compounds **1i** and **12a**

Figure 44. Antiproliferative Activity comparing (A) huMy9-6-SPDB-**1f**, (B) huMy9-6-sulfoSPDB-**1f**, and, (C) huMy9-6-BMPS-**1f** against OCI-AML3 (Ag^+) cells with and without blocking of antigen binding sites

A)





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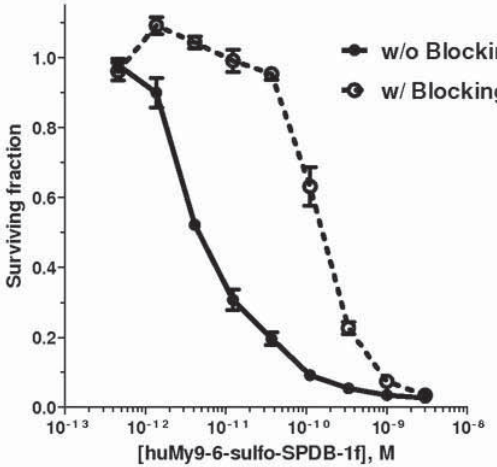

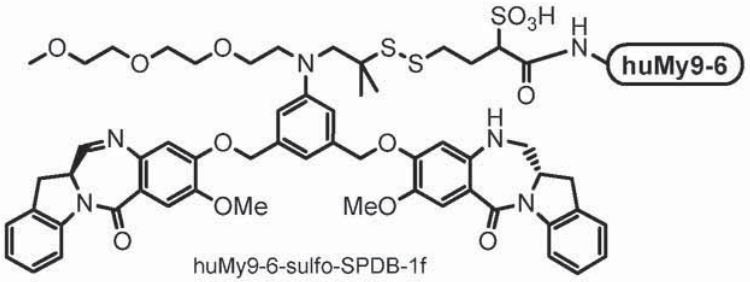

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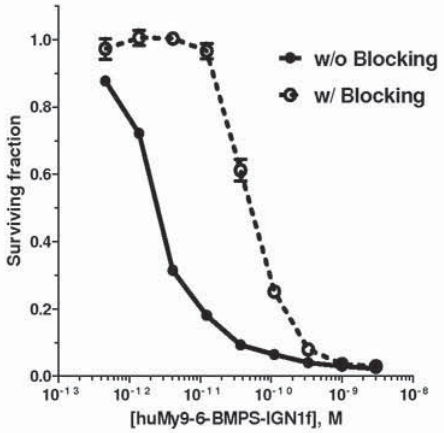


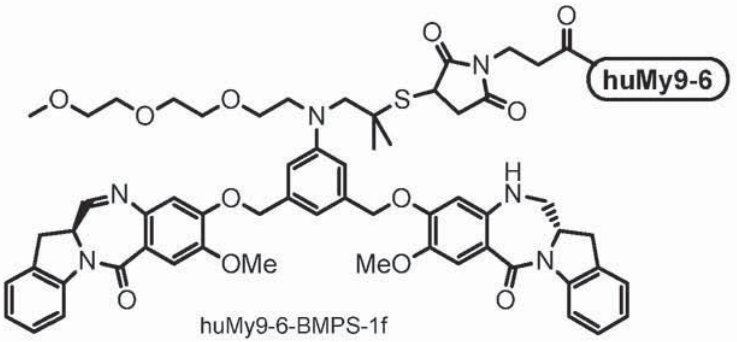


Figure 45. Alternate Synthsis of 4-(benzyloxy)-5-methoxy-2-nitrobenzoic acid used in the Preperation of IBD Monomer

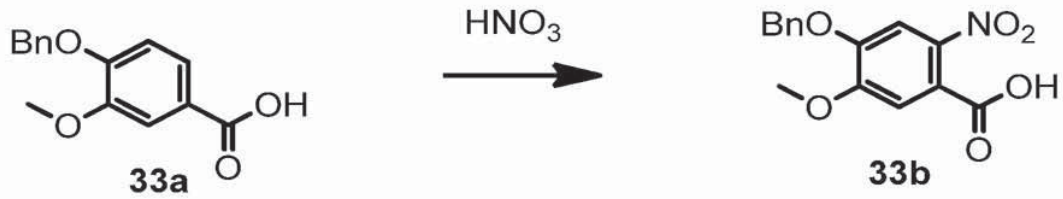


Figure 46. Alternate Synthesis of (5-((2-(2-(2-methoxyethoxy)ethoxy)ethyl)(2-methyl-2-(methyldisulfanyl)propyl)amino)-1,3-phenylene)dimethanol (**1b**)

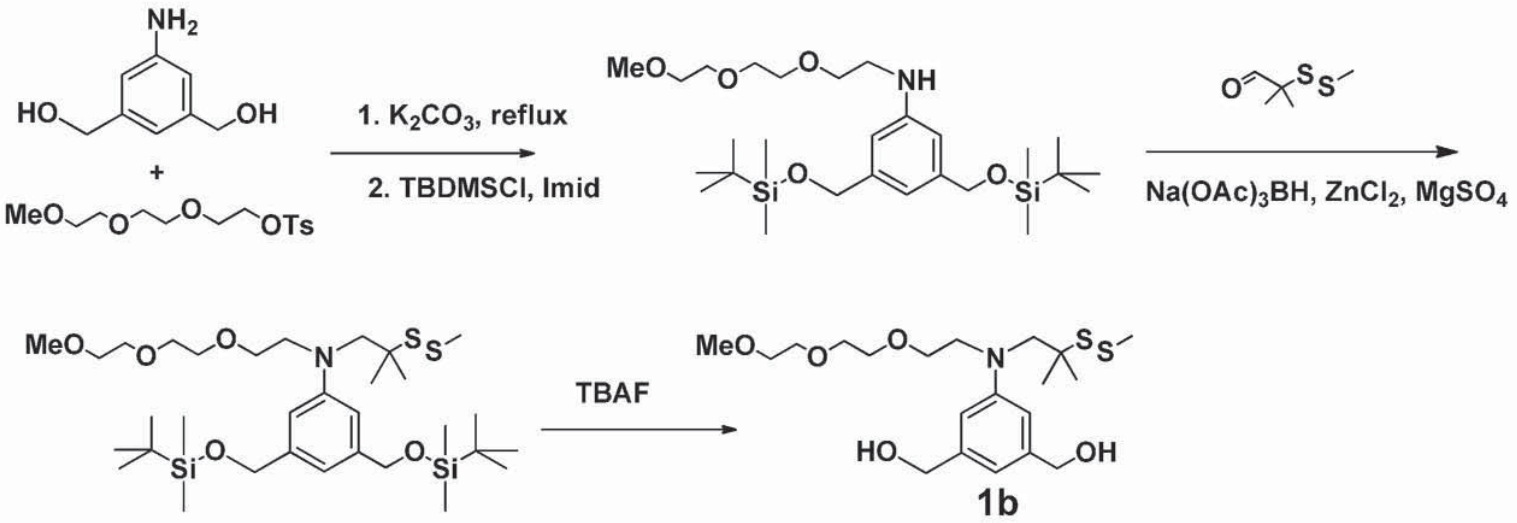


Figure 47. Alternate Synthesis of (5-((2-(2-(2-methoxyethoxy)ethoxy)ethyl)(2-methyl-2-(methyldisulfanyl)propyl)amino)-1,3-phenylene)dimethanol (**1b**)

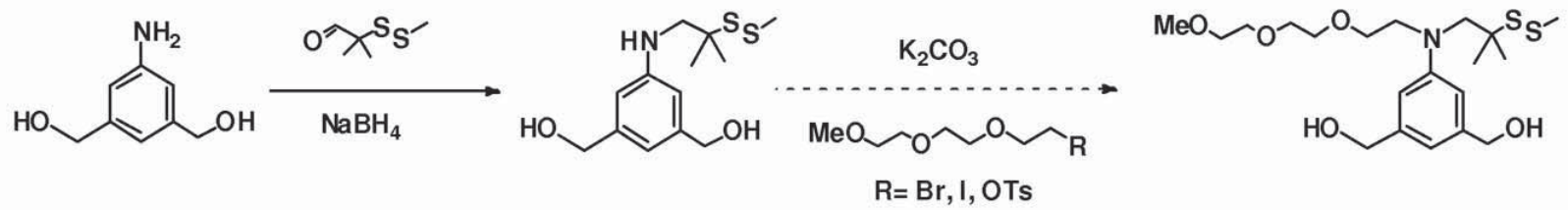


Figure 48. Alternate Synthetic Scheme for a Two-step Mono-imine Dimer Synthesis

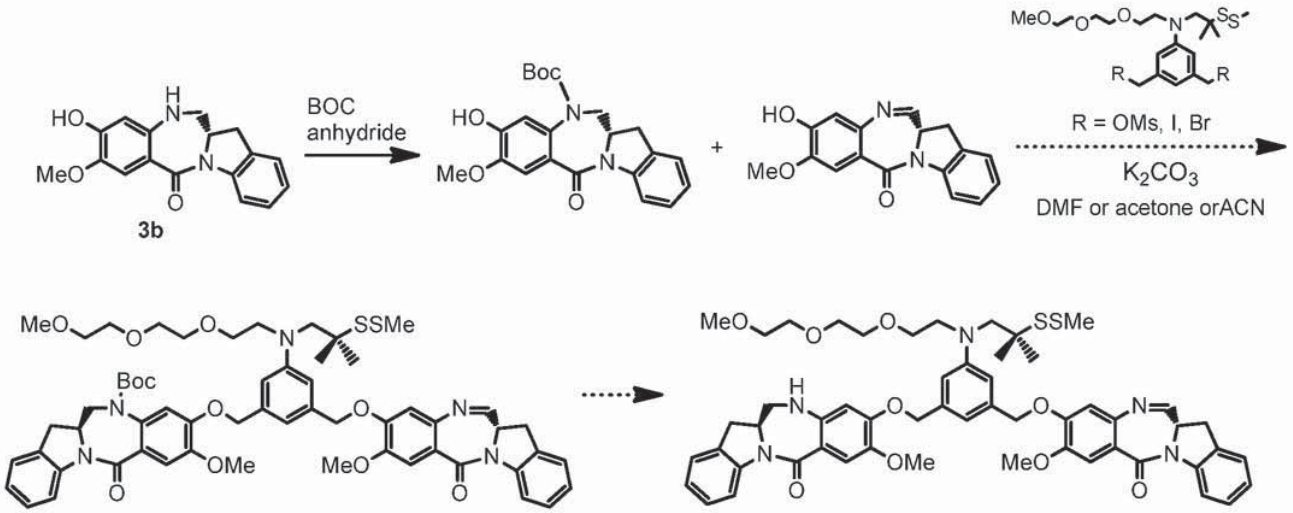
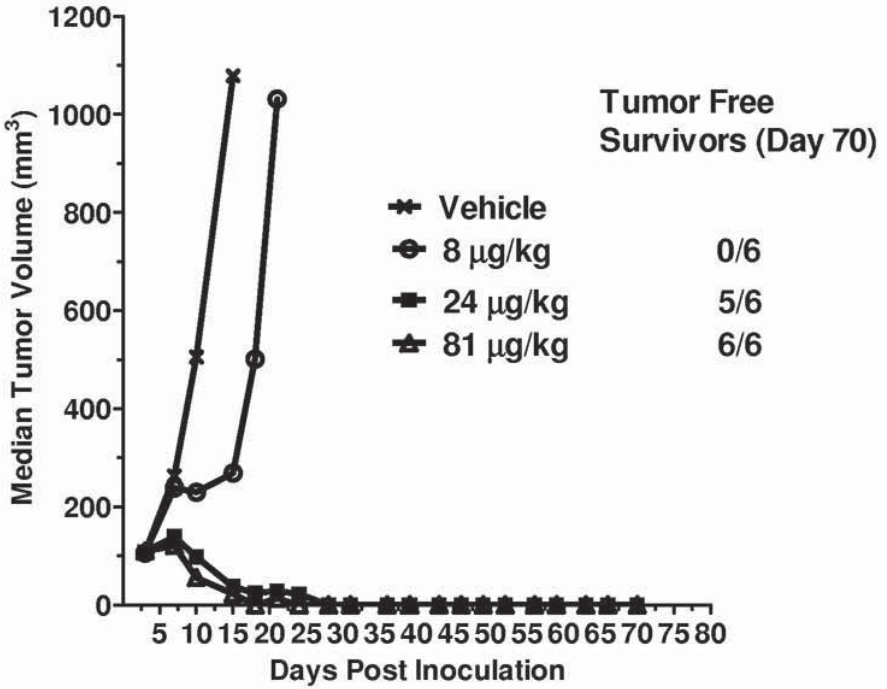


Figure 49. Potency of Conjugates against Various Cell Lines Measured by IC_{50} values (nM)

conjugate	HL60/QC	MOLM-13	NB4	HEL92.1.7	OCI-AML3
huMy9-6-SPDB-1f	0.005	0.003	0.3	0.5	0.01
huMy9-6-sulfo-SPDB-1f	0.006	0.002	0.4	0.05	0.008
huMy9-6-BMPS-1f	0.003	0.001	0.04	0.04	0.003

Figure 50. *In Vivo* Efficacy of huMy9-6-sulfo-SPDB-**1f** in MOLM-13 Tumor Bearing Mice



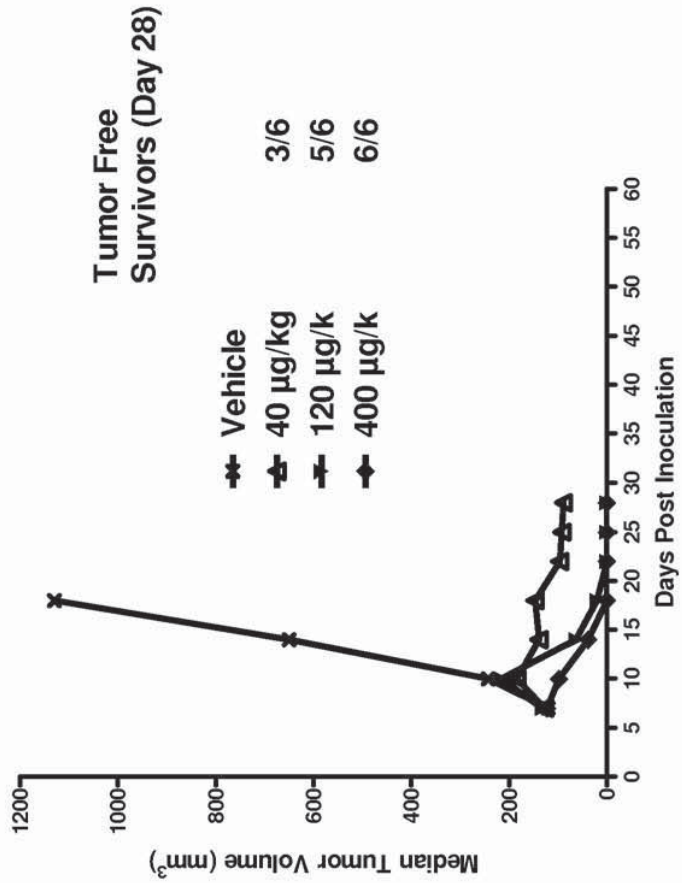


Figure 51. *In Vivo* Efficacy of huMy9-6-sulfo-SPDB-**1f** in NB4 Tumor Bearing Mice

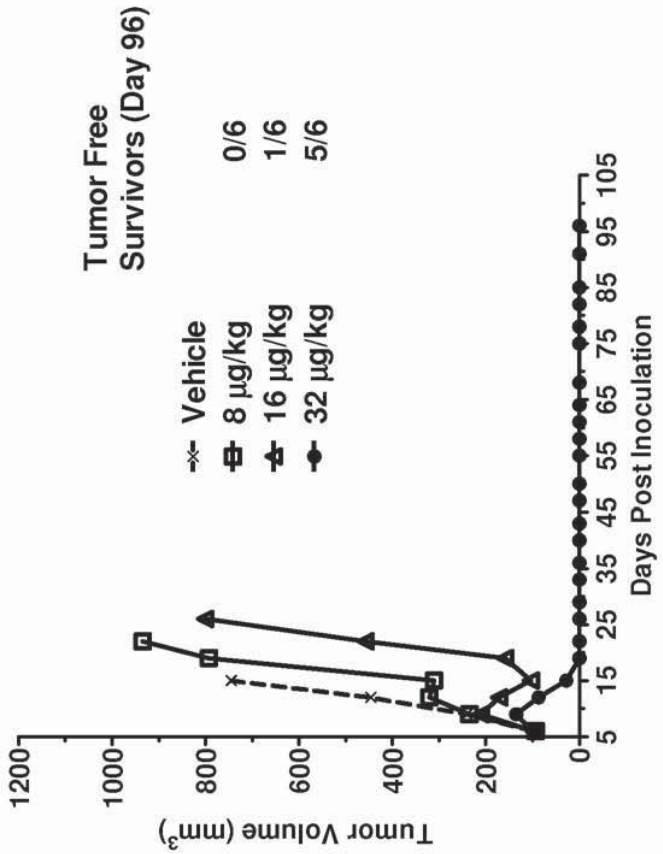


Figure 52. *In Vivo* Efficacy of huMy9-6-BMPS-**1f** in HL60/QC Tumor Bearing Mice

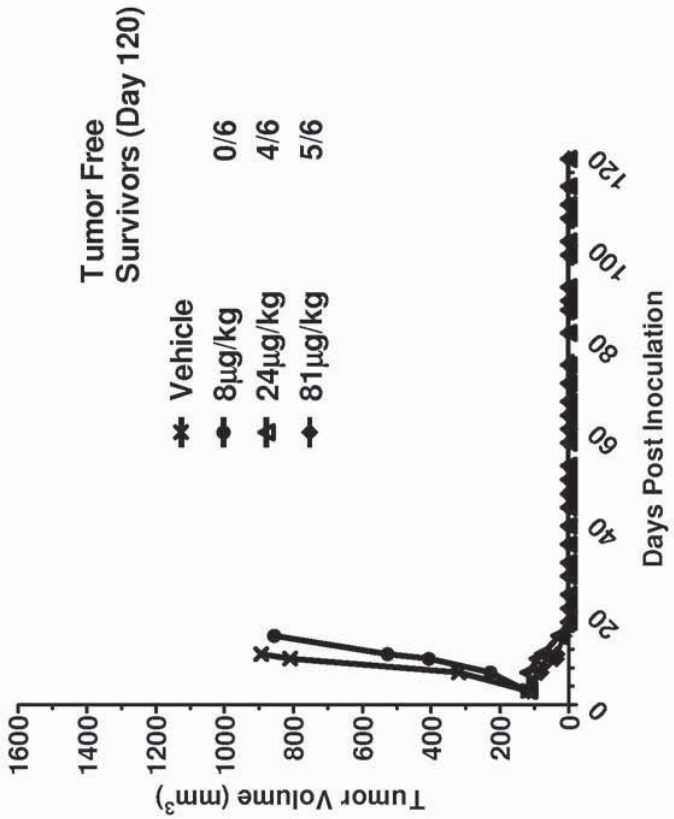


Figure 53. *In vivo* Efficacy of huMy9-6-BMPS-**1f** in MOLM-13 Tumor Bearing Mice

Figure 54. Representative Synthesis Scheme for a Sulfonated Folate / Cytotoxic Compound Conjugate

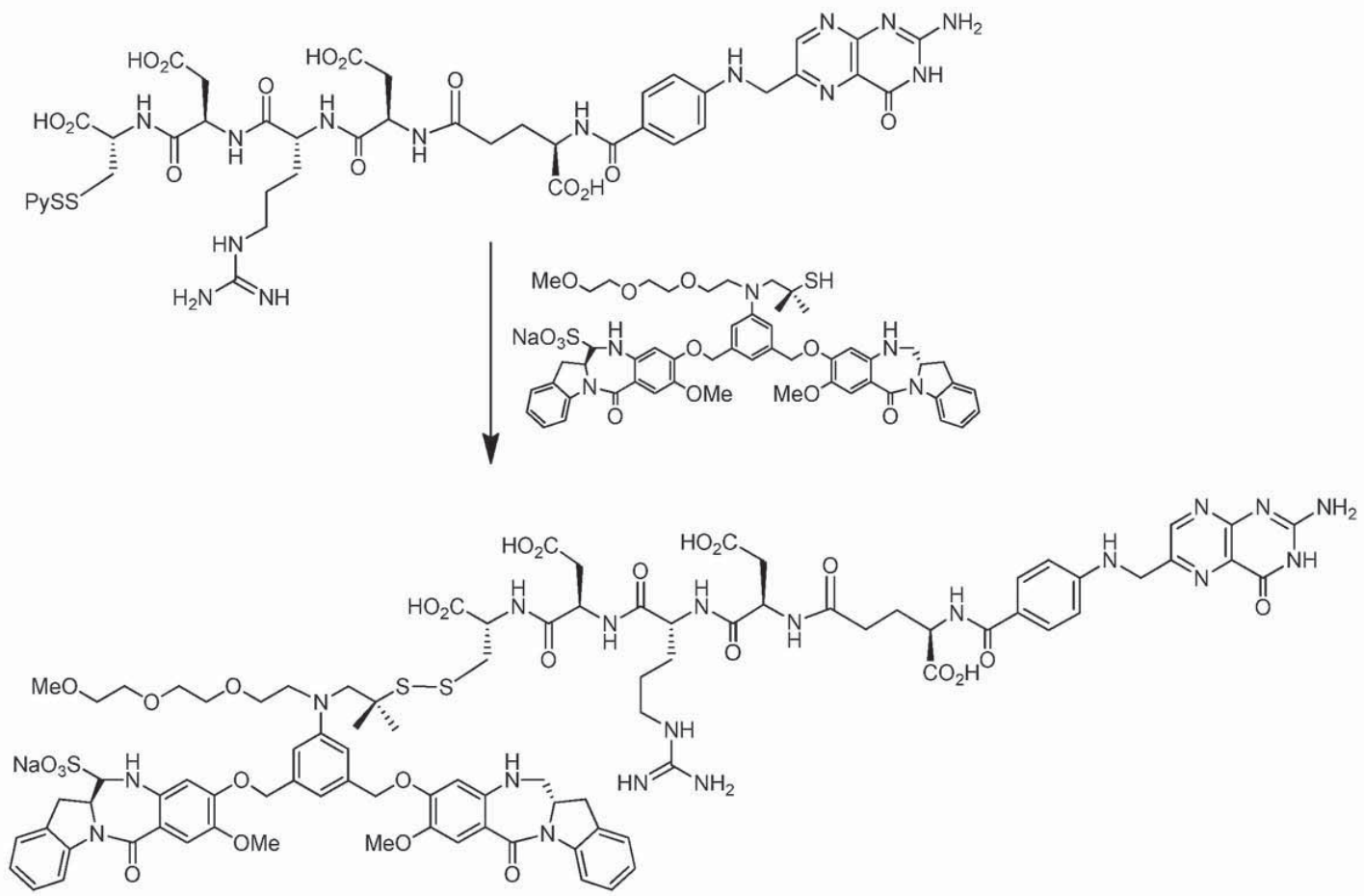
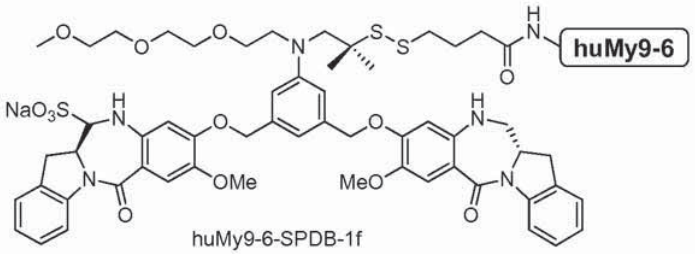
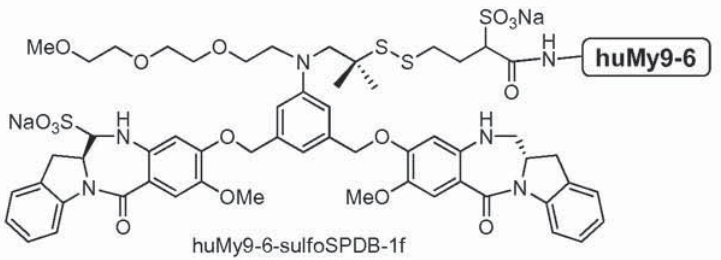


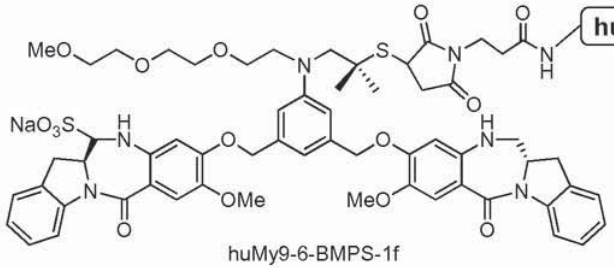
Figure 55. Structures of Several Sulfonated Drug-Antibody (huMy9-6) Conjugates



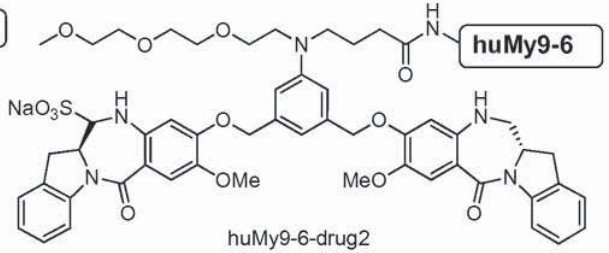
huMy9-6-SPDB-1f



huMy9-6-sulfoSPDB-1f



huMy9-6-BMPS-1f



huMy9-6-drug2

Figure 56. *In vivo* Efficacy of huMy9-6-drug2 in HL60/QC Tumor Bearing Mice

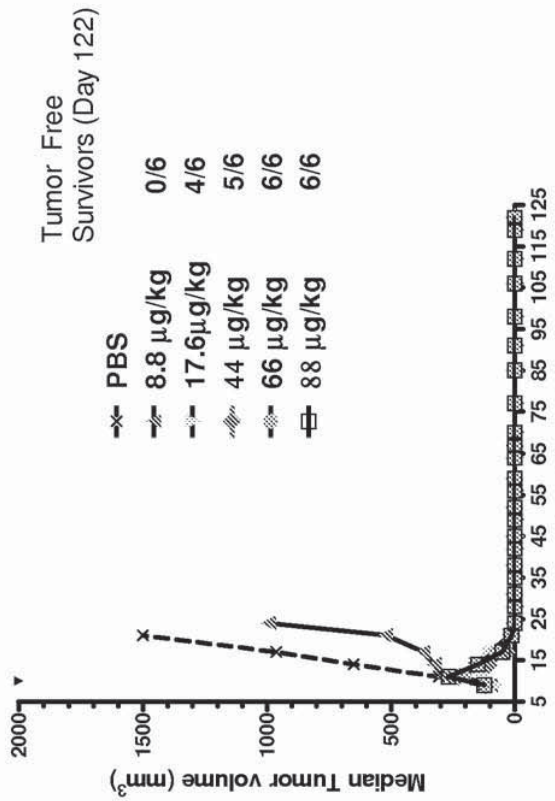


Figure 57. *In vivo* Efficacy of huMy9-6-drug2 in MOLM-13 Tumor Bearing Mice

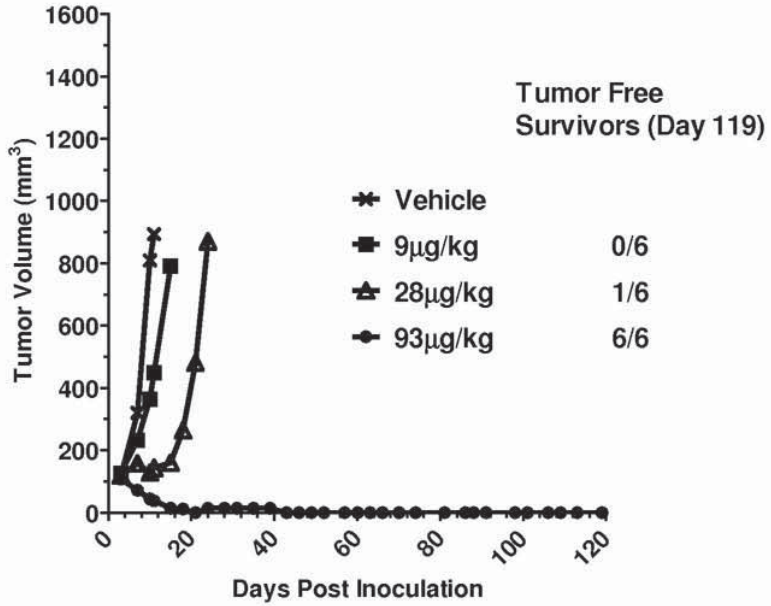


Figure 58.

HuMy9-6-2 conjugates prepared without and with sodium bisulfite show similar *in vitro* cytotoxicity toward CD33-antigen expressing HL60 cells

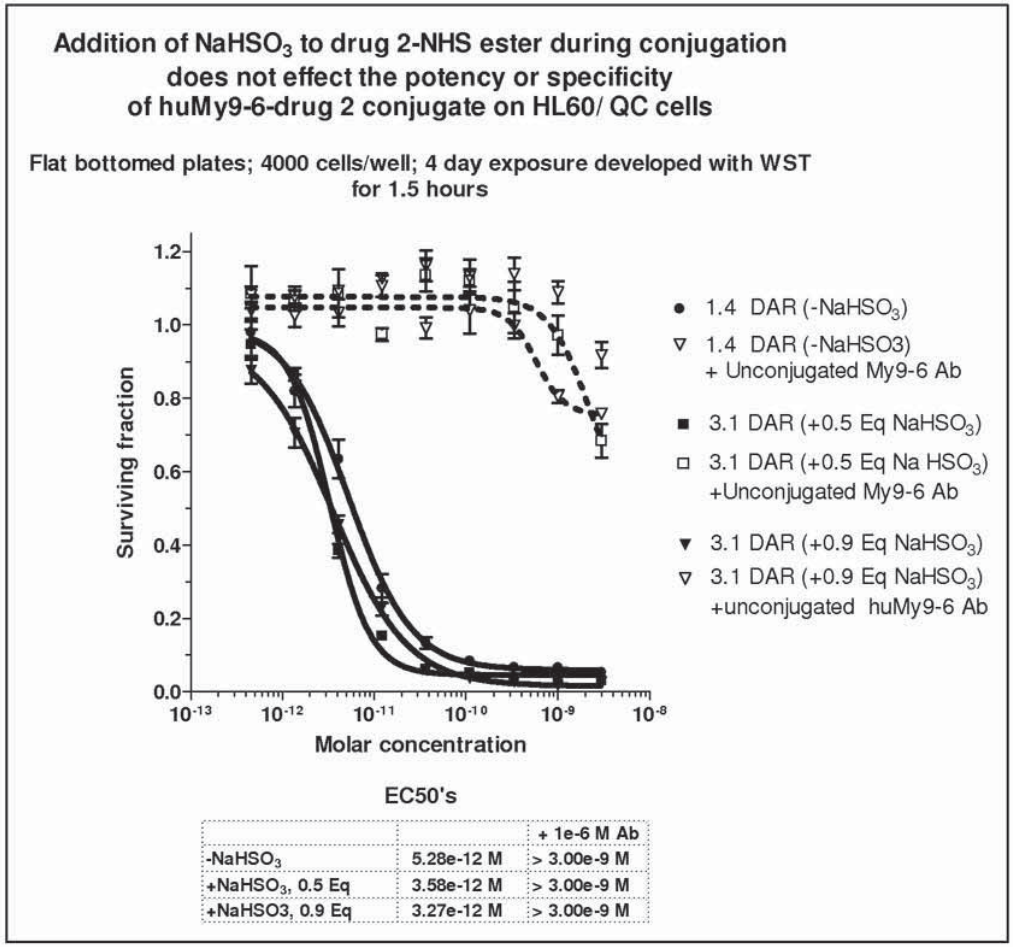
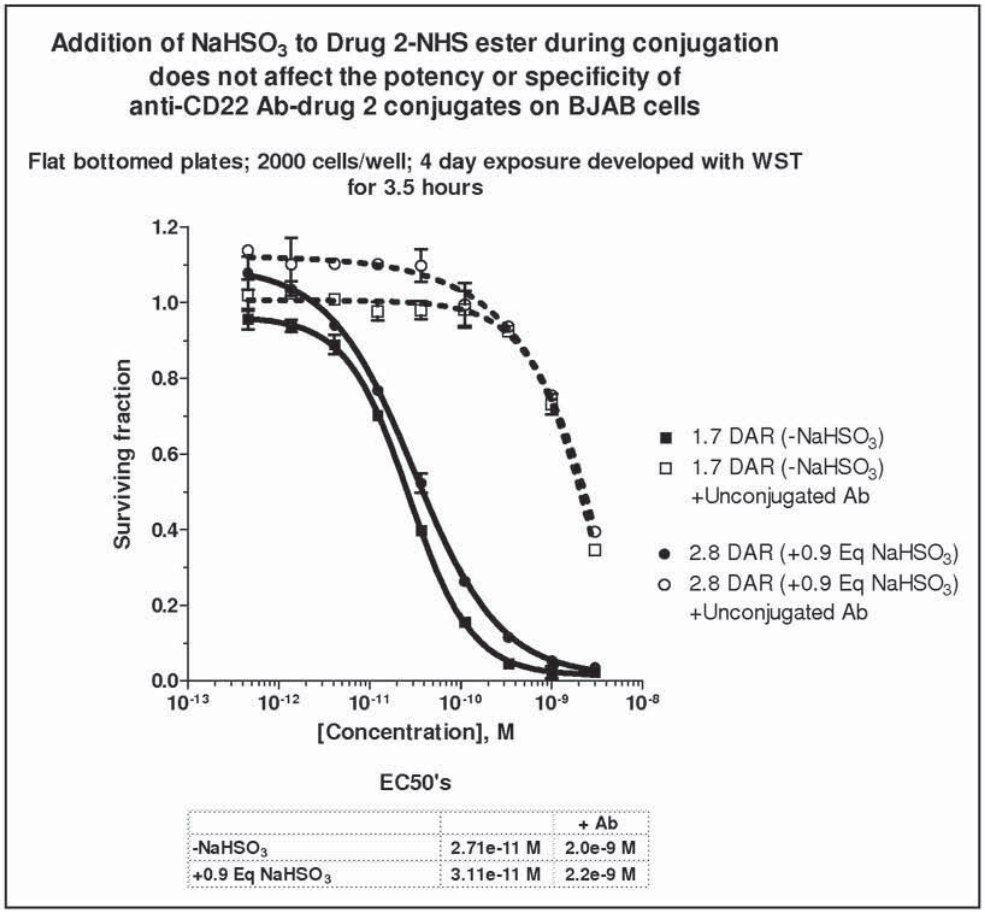


Figure 59.

Anti-CD22 Ab-2 conjugates prepared without and with sodium bisulfite show similar *in vitro* cytotoxicity toward CD22-antigen expressing BJAB cells.



		+ Ab
-$NaHSO_3$	2.71e-11 M	2.0e-9 M
+0.9 Eq $NaHSO_3$	3.11e-11 M	2.2e-9 M

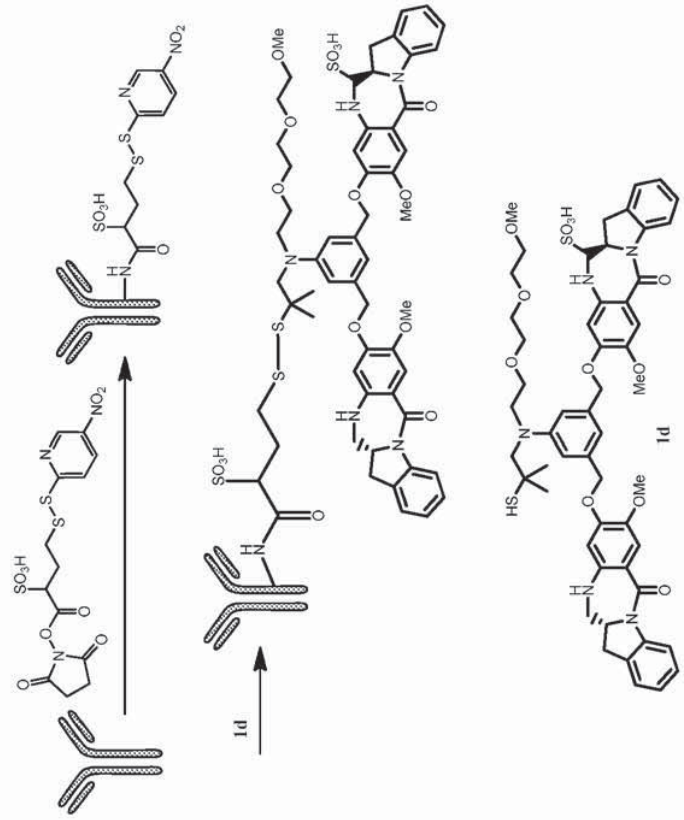



Figure 60.