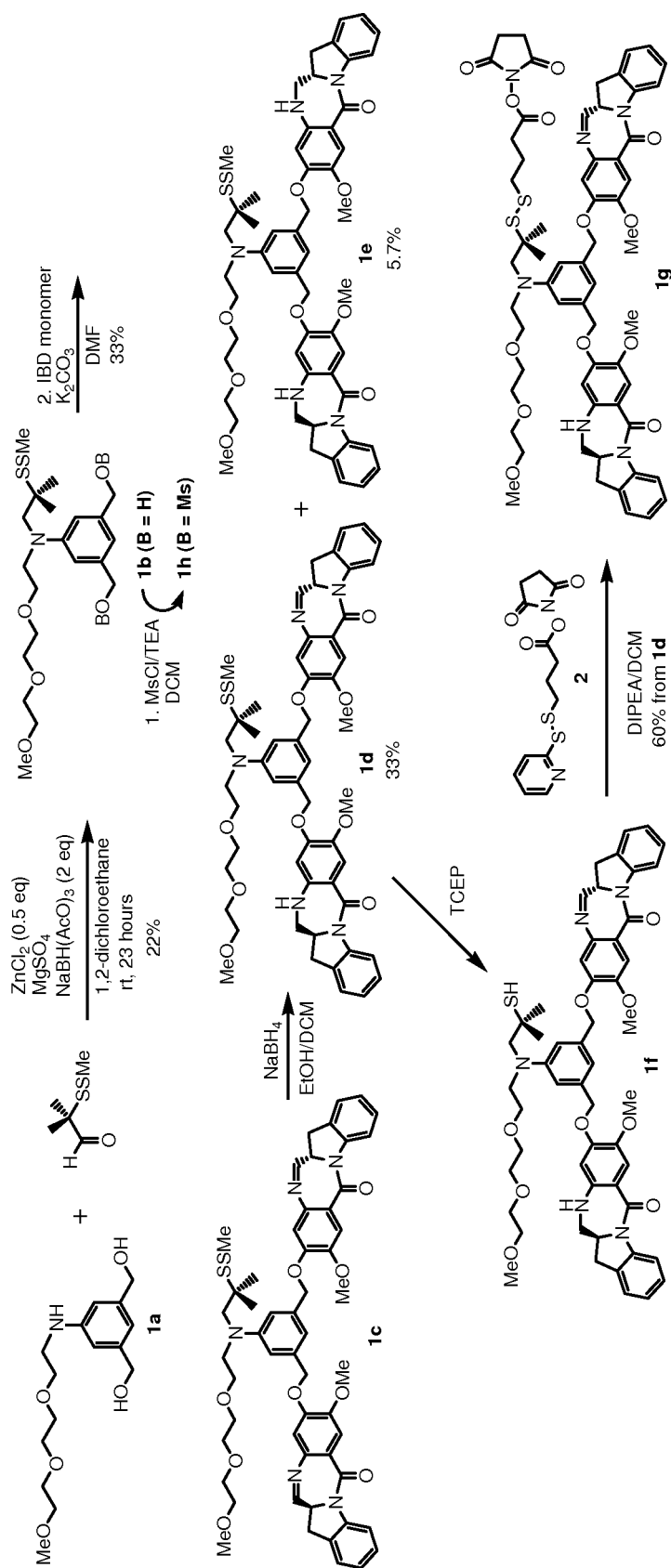


Figure 1. Synthetic Scheme of Linker **1b** and Dimers **1d-g**

Chemical reaction scheme showing the synthesis of compound **2b** from compound **1c**.

Compound **1c** is converted to compound **1e** using $\text{NaBH}(\text{AcO})_3$ in 1,2-dichloroethane, yielding **1e** in 58% yield.

Compound **1e** is converted to compound **2a** using TCEP, yielding **2a** in 43% yield.

Compound **2a** is converted to compound **2b** using compound **2** in the presence of DIPEA/DCM.

Reaction scheme for the synthesis of IBD monomers 3a-f:

3a $\xrightarrow{\text{H}_2, \text{Pd}}$ 3b (98% yield)

3b $\xrightarrow{\text{NaBH}(\text{AcO})_3}$ 3c (43% yield)

3c $\xrightarrow{\text{K}_2\text{CO}_3, \text{DMF}}$ 3d (58% yield)

3d + I-alkane $\rightarrow$ 3e

3d $\xrightarrow{\text{TCEP}}$ 3f

3f + 2 $\xrightarrow{\text{DIPEA/CH}_2\text{Cl}_2}$ 3g (38% from 3e)

Figure 4. Synthetic Scheme of Dimers 4b-e

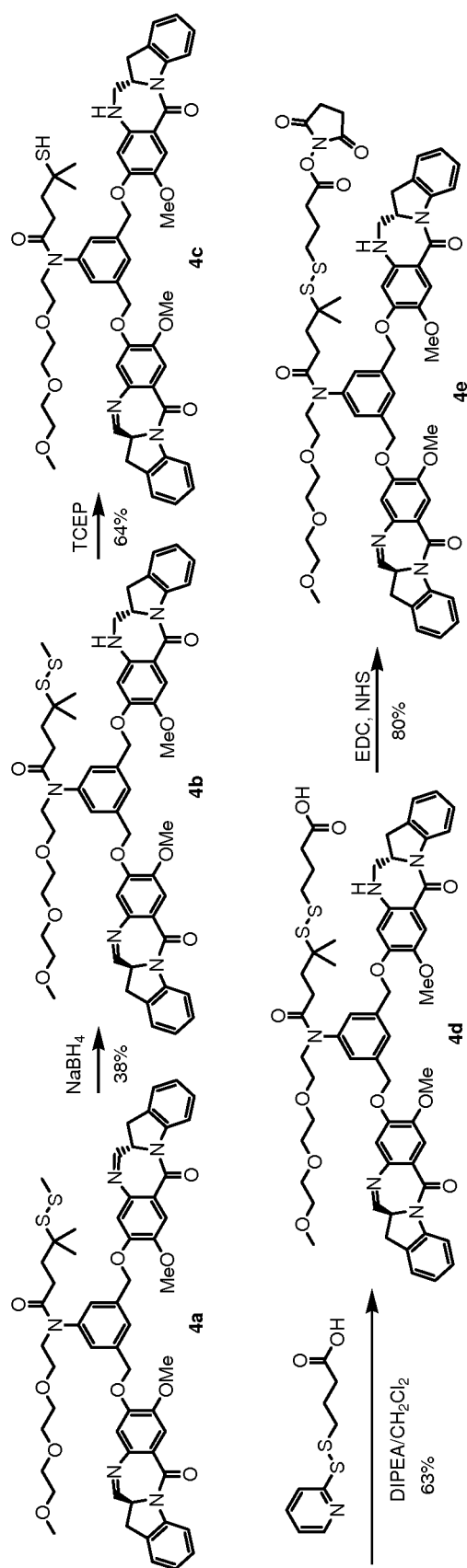


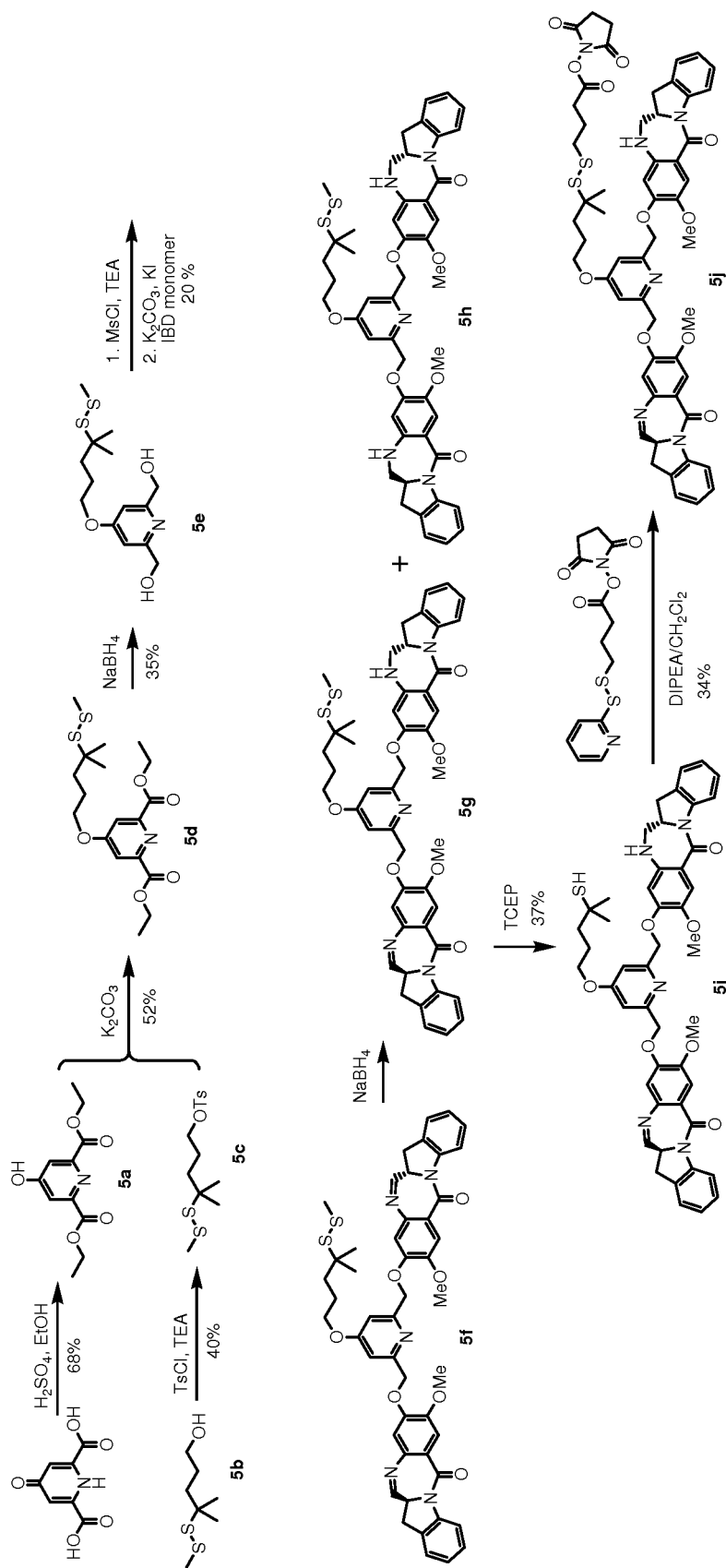
Figure 5. Synthetic Scheme of Linker **5e** and Dimers **5g-j**

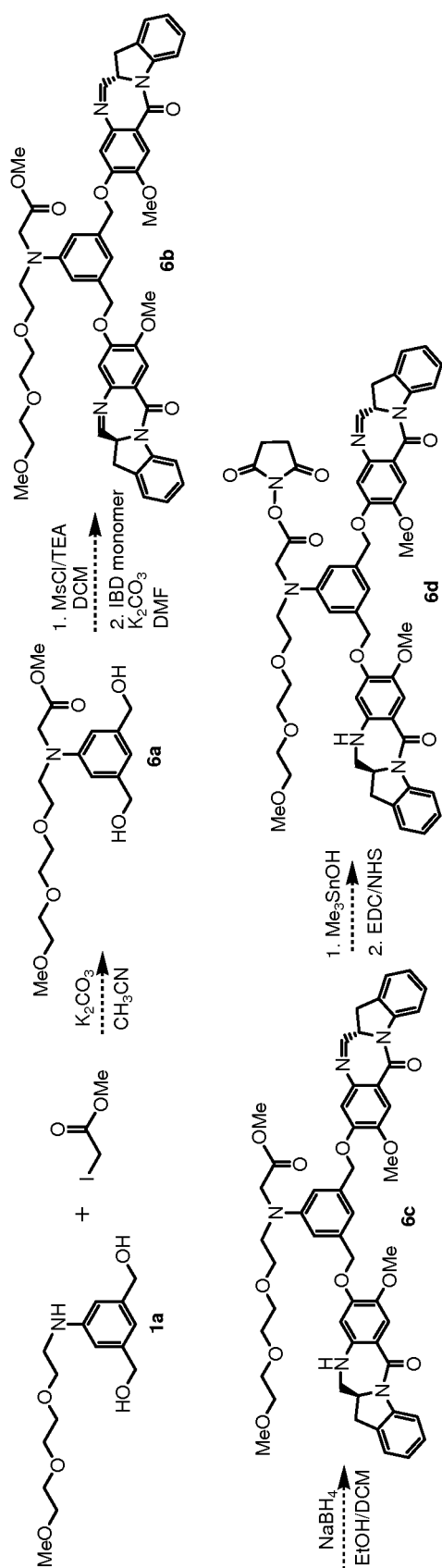
Figure 6. Synthetic Scheme of Linker **6a** and Dimers **6c-d**

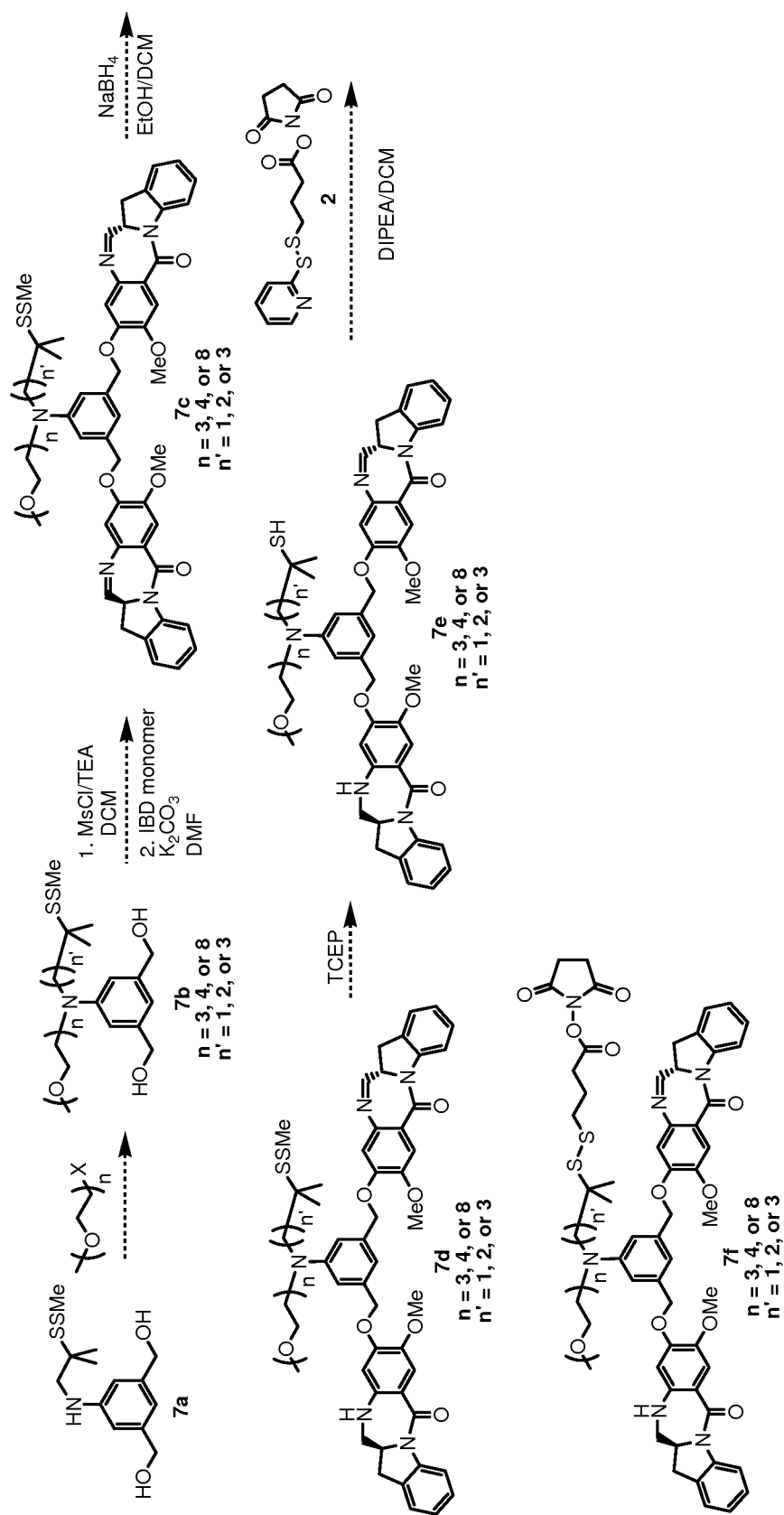
Figure 7. Synthetic Scheme of PEG Modified Linkers **7b** and Dimers **7d-f**

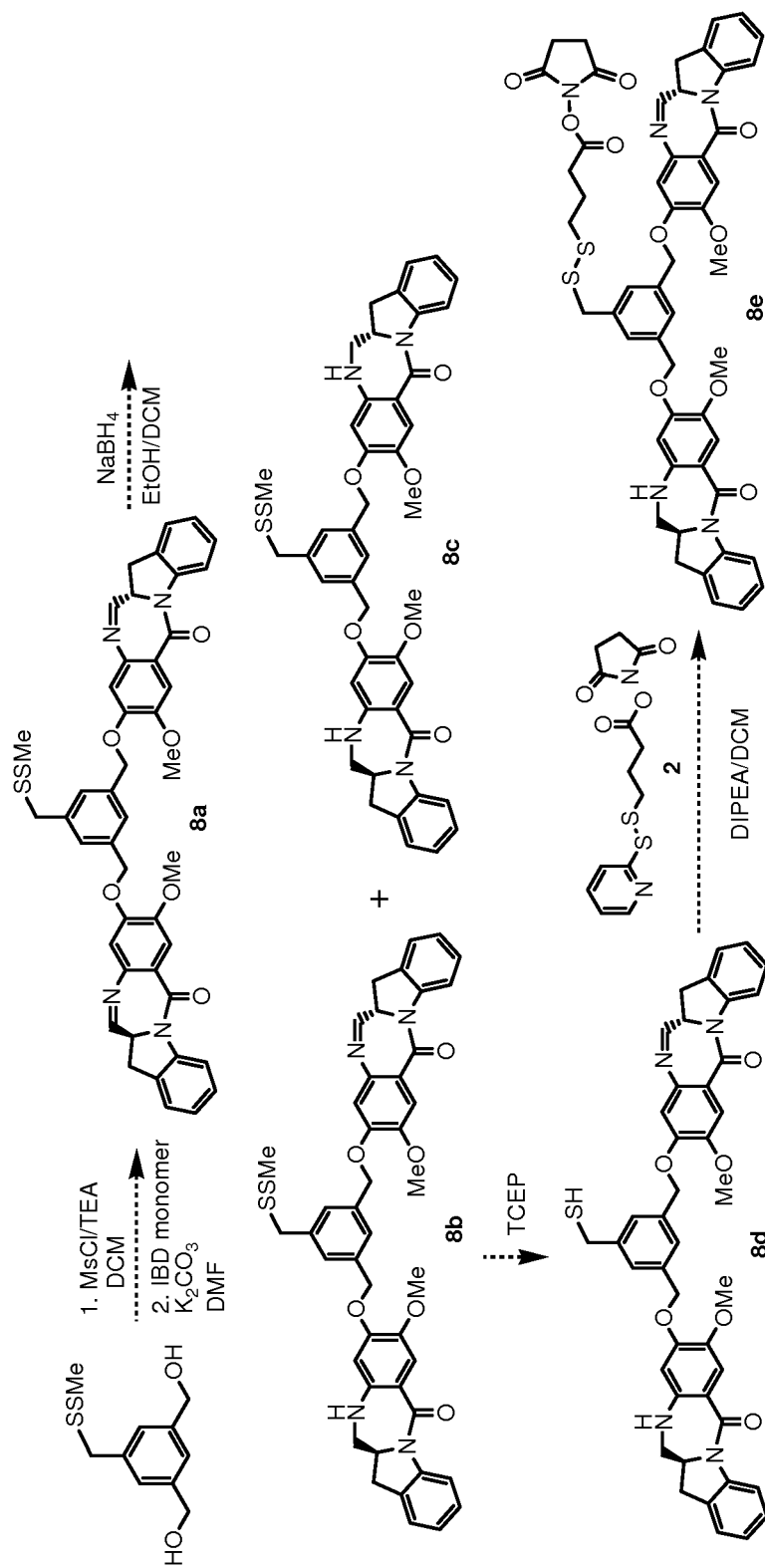
Figure 8. Synthetic Scheme of Thiol-containing Dimers **8b-e**

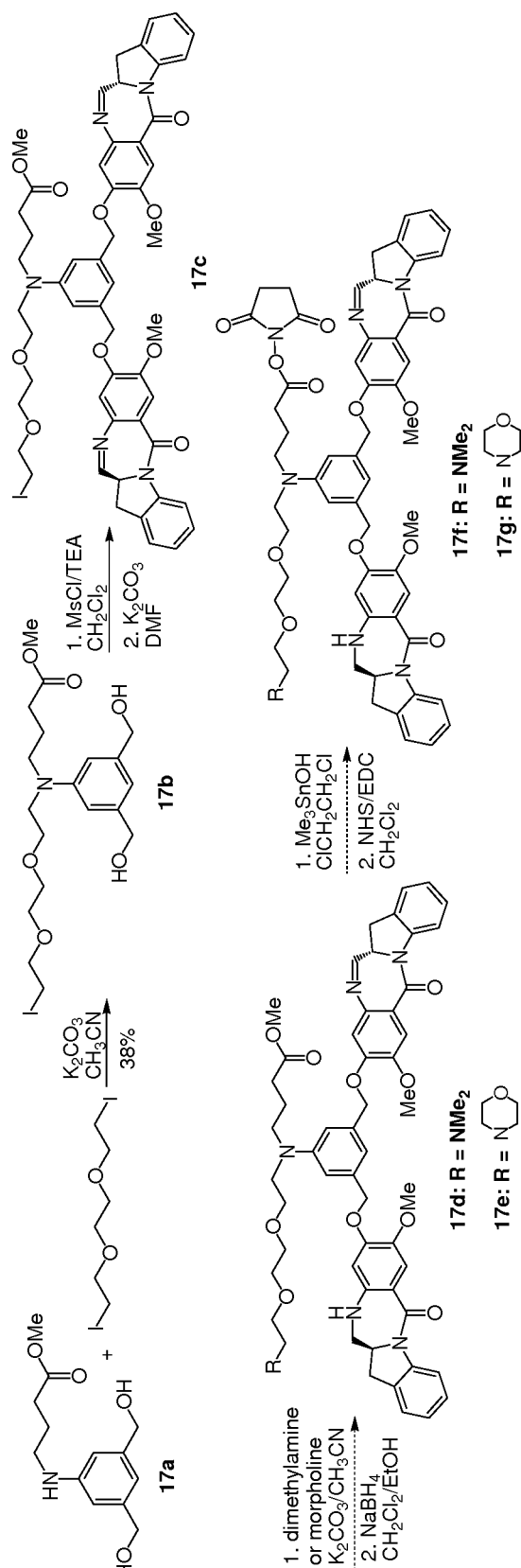
Figure 9. Synthetic Scheme of Dimers **17d-g** Containing a Tertiary Amine

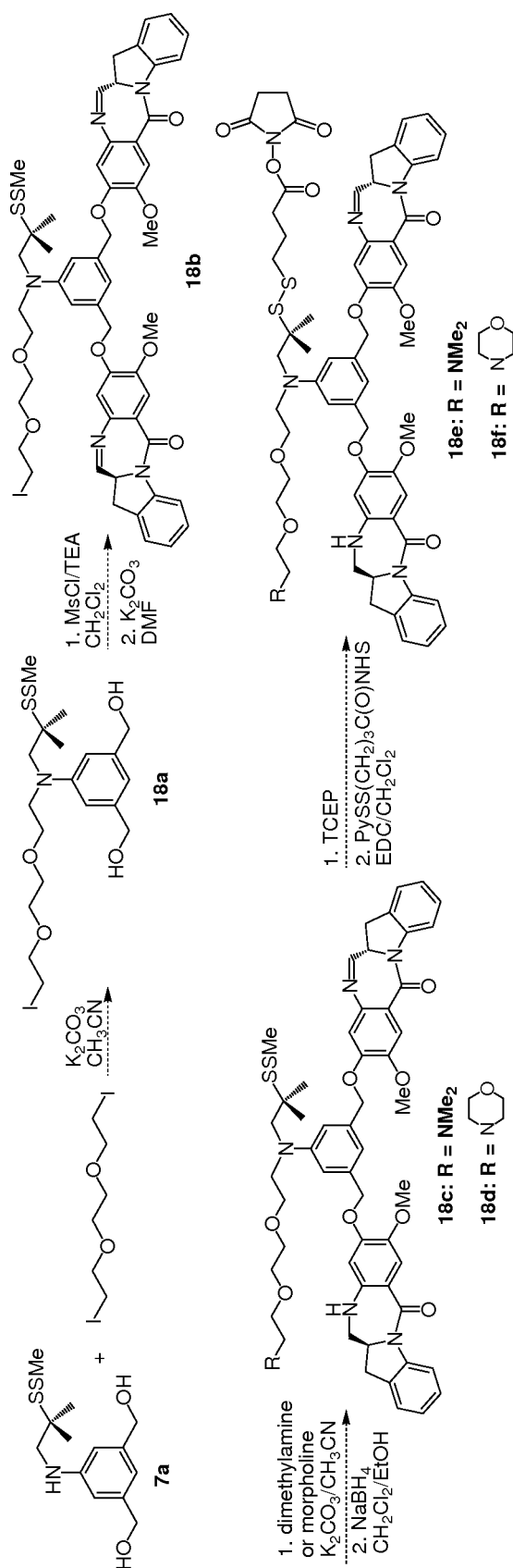
Figure 10. Synthetic Scheme of Dimers **18c-f** Containing a Tertiary Amine

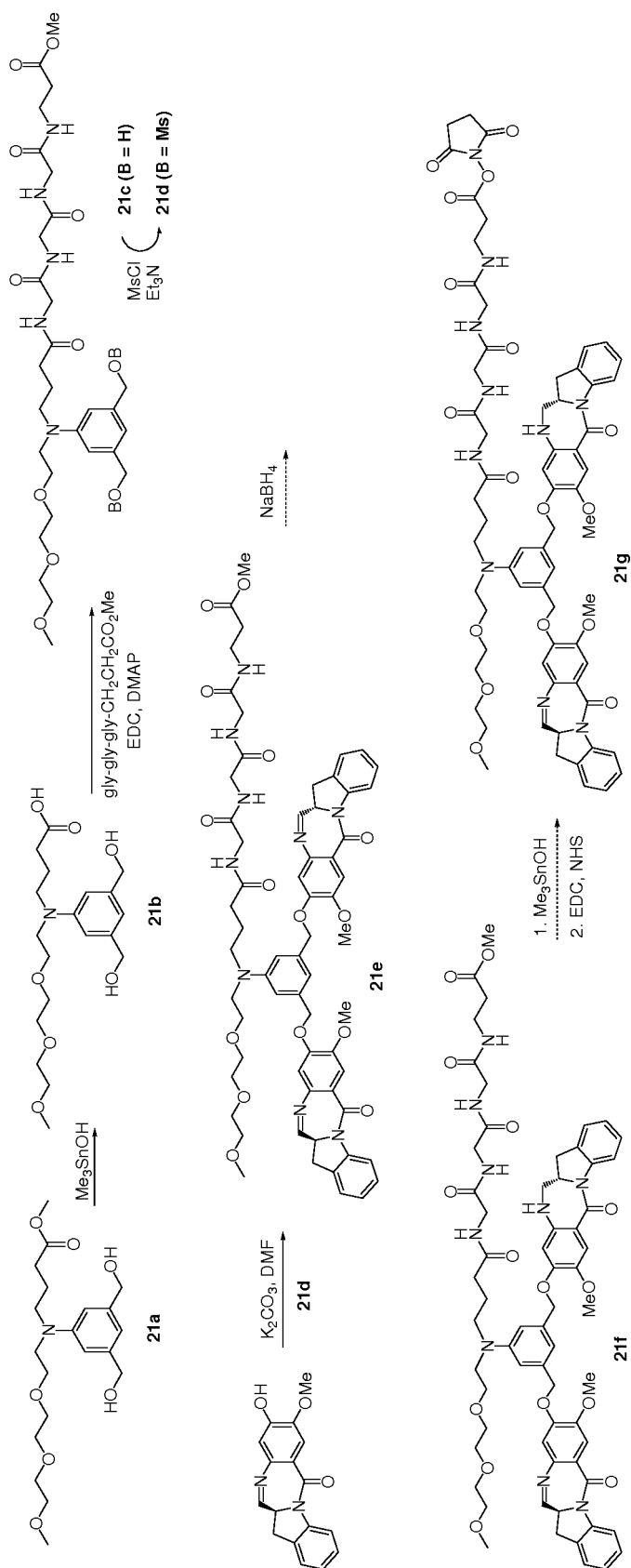
Figure 11. Synthetic Scheme of Dimers **21f-g** Containing a Peptide Linker

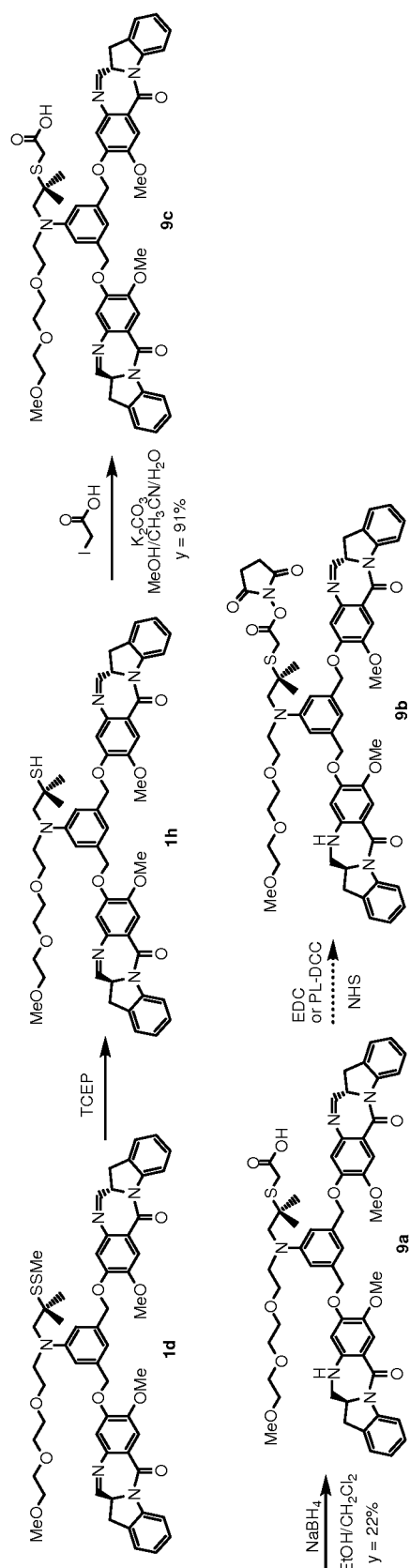
Figure 12A. Synthetic Scheme of the One-step Thioacetyl Linkable Dimers **9a-b**

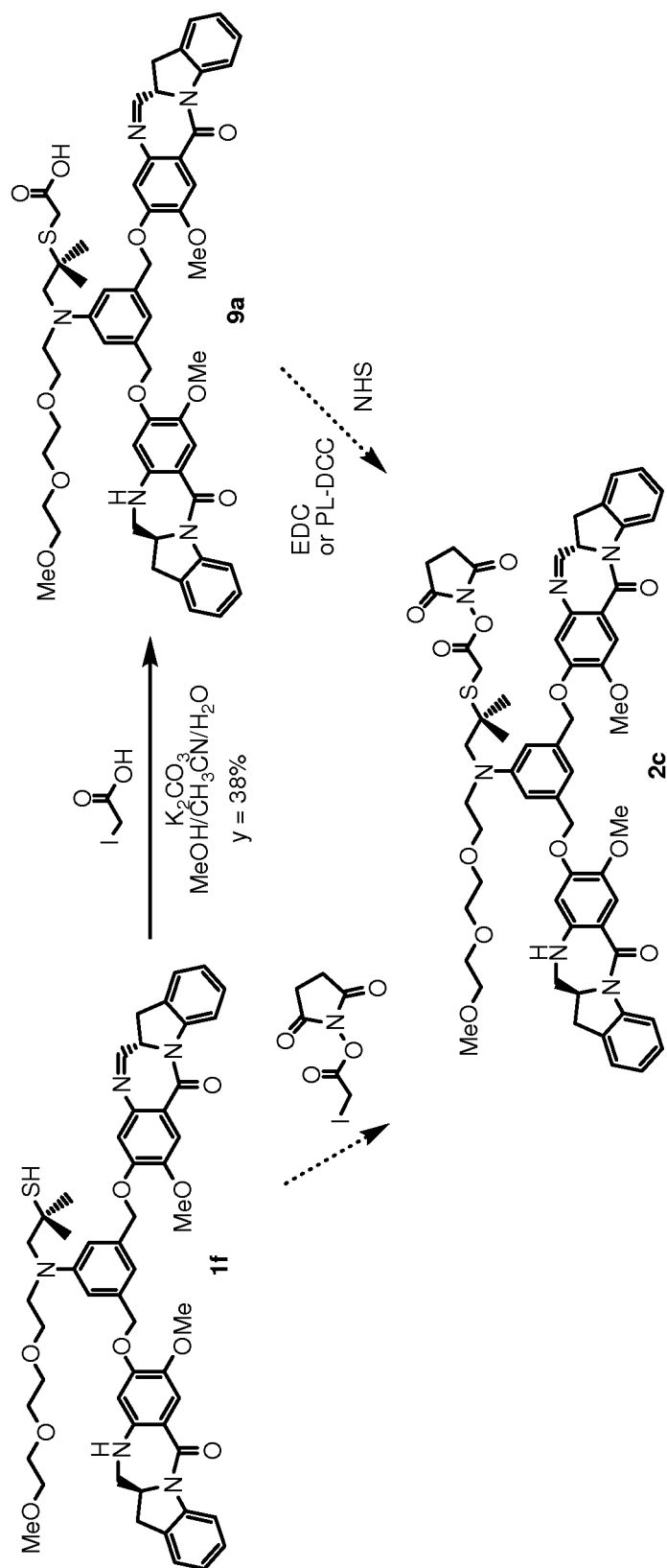
Figure 12B. Alternative Synthetic Scheme of the One-step Thioacetyl Linkable Dimers **9a-b**

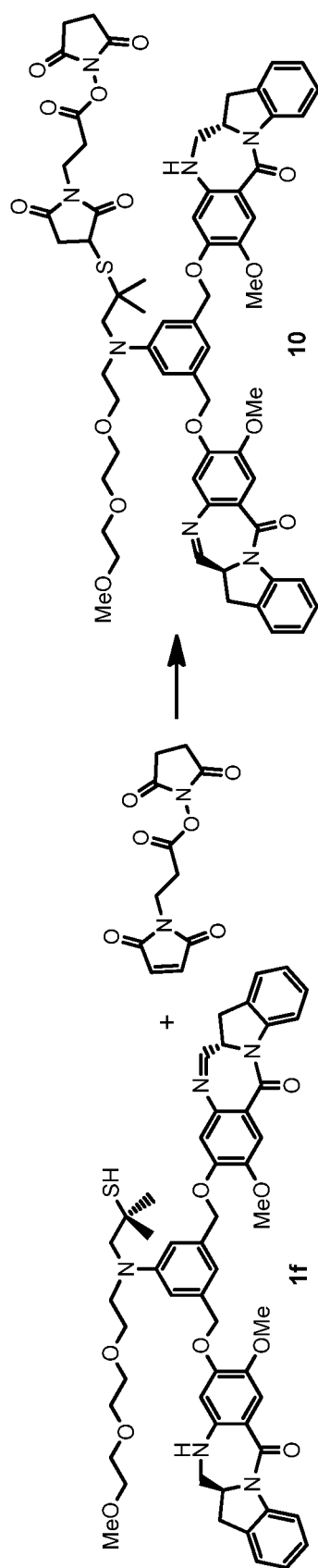
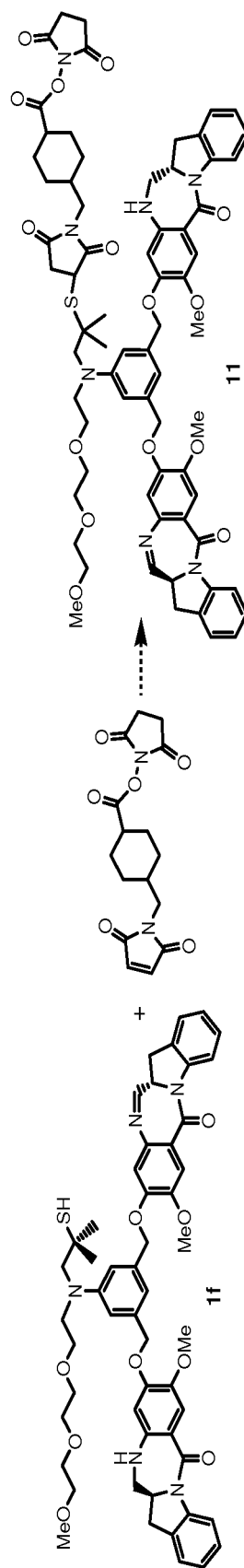
Figure 13. Synthetic Scheme of the One-step BMPS Linkable Dimer **10**Figure 14. Synthetic Scheme of the One-step SMCC Linkable Dimer **11**

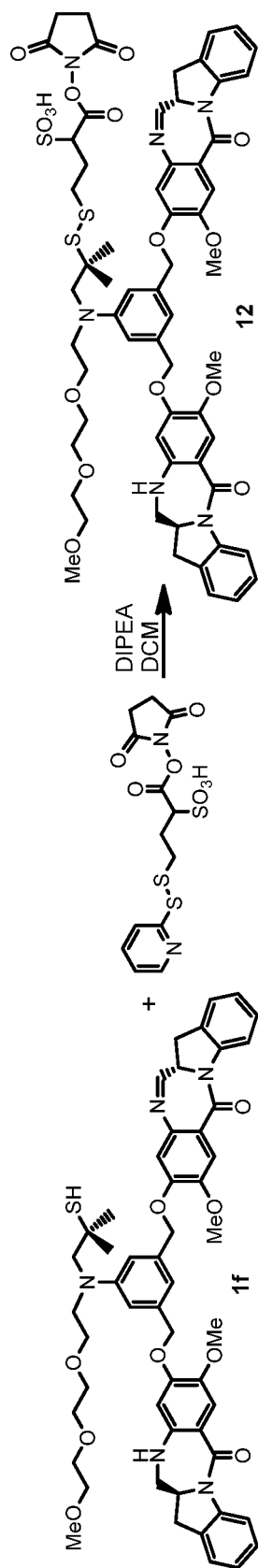
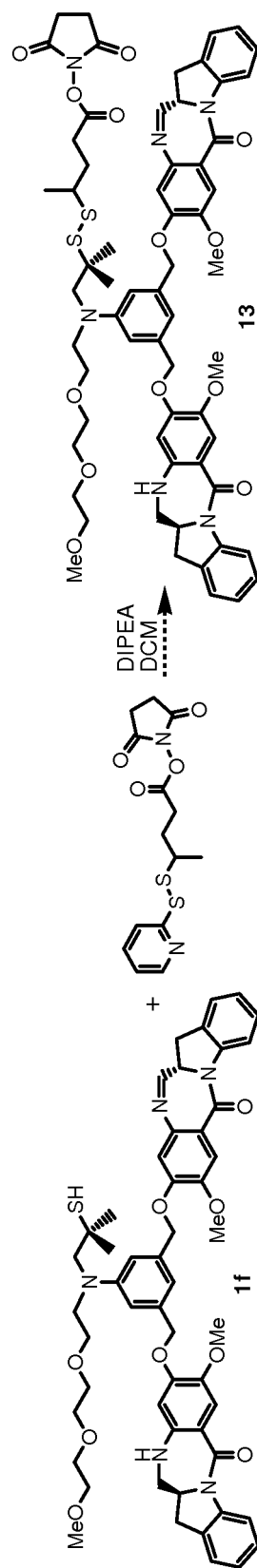
Figure 15. Synthetic Scheme of the One-step Sulfo-SPDB Linkable Dimer **12**Figure 16. Synthetic Scheme of the One-step SPP Linkable Dimer **13**

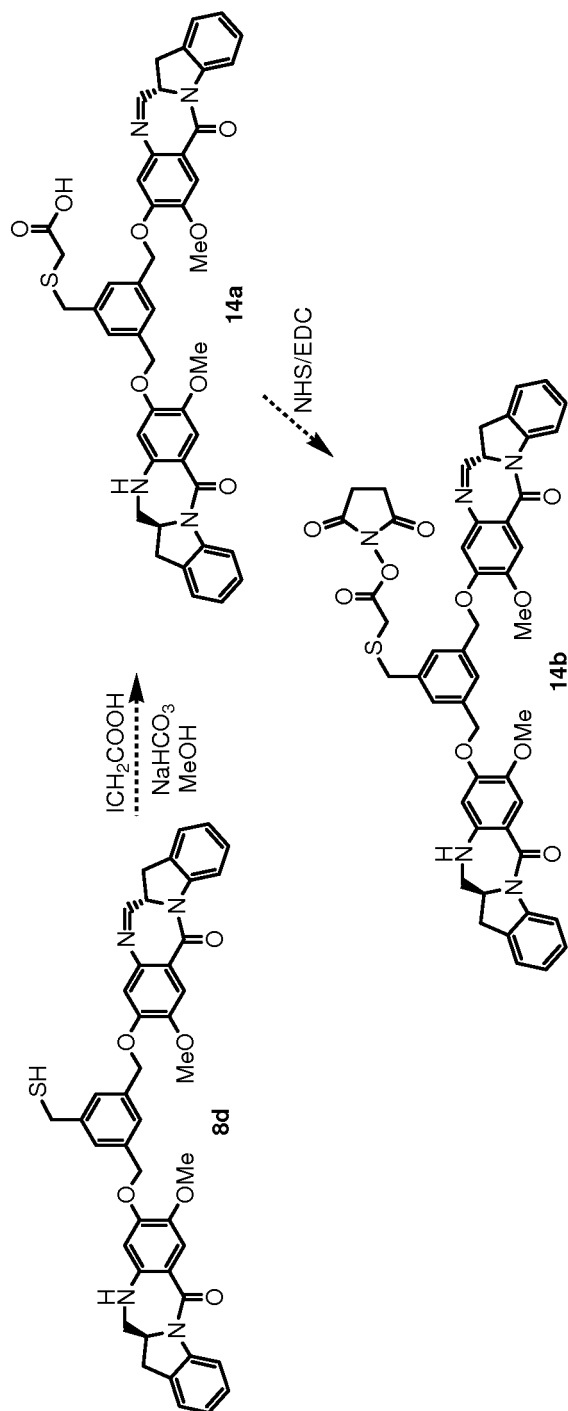
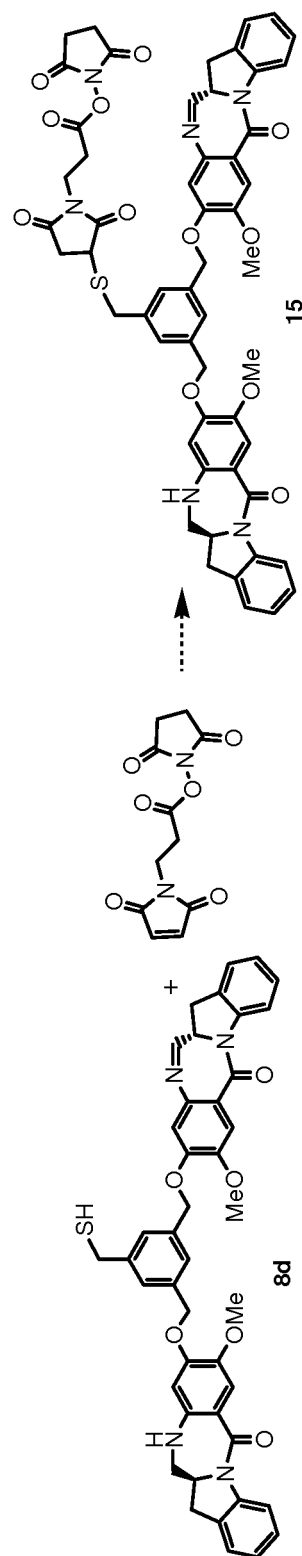
Figure 17. Synthetic Scheme of the One-step Thioacetyl Linkable Dimers **14a-b**Figure 18. Synthetic Scheme of the One-step BMPS Linkable Dimer **15**

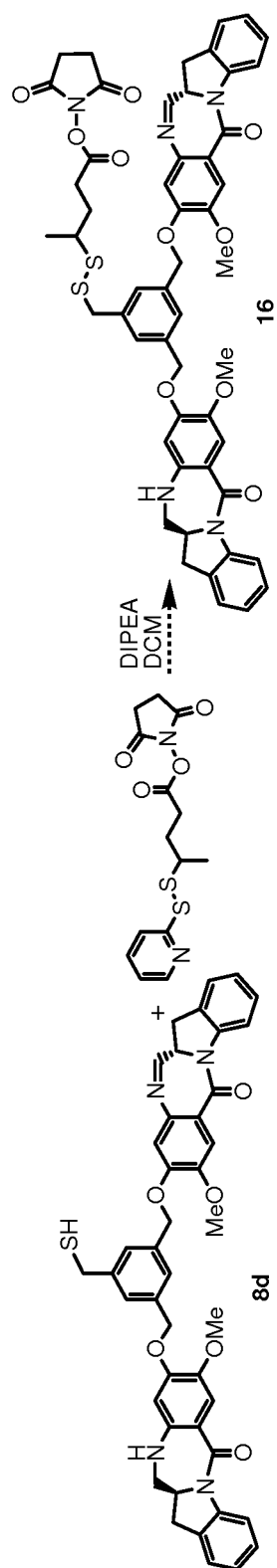
Figure 19. Synthetic Scheme of the One-step SPP Linkable Dimer **16**

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

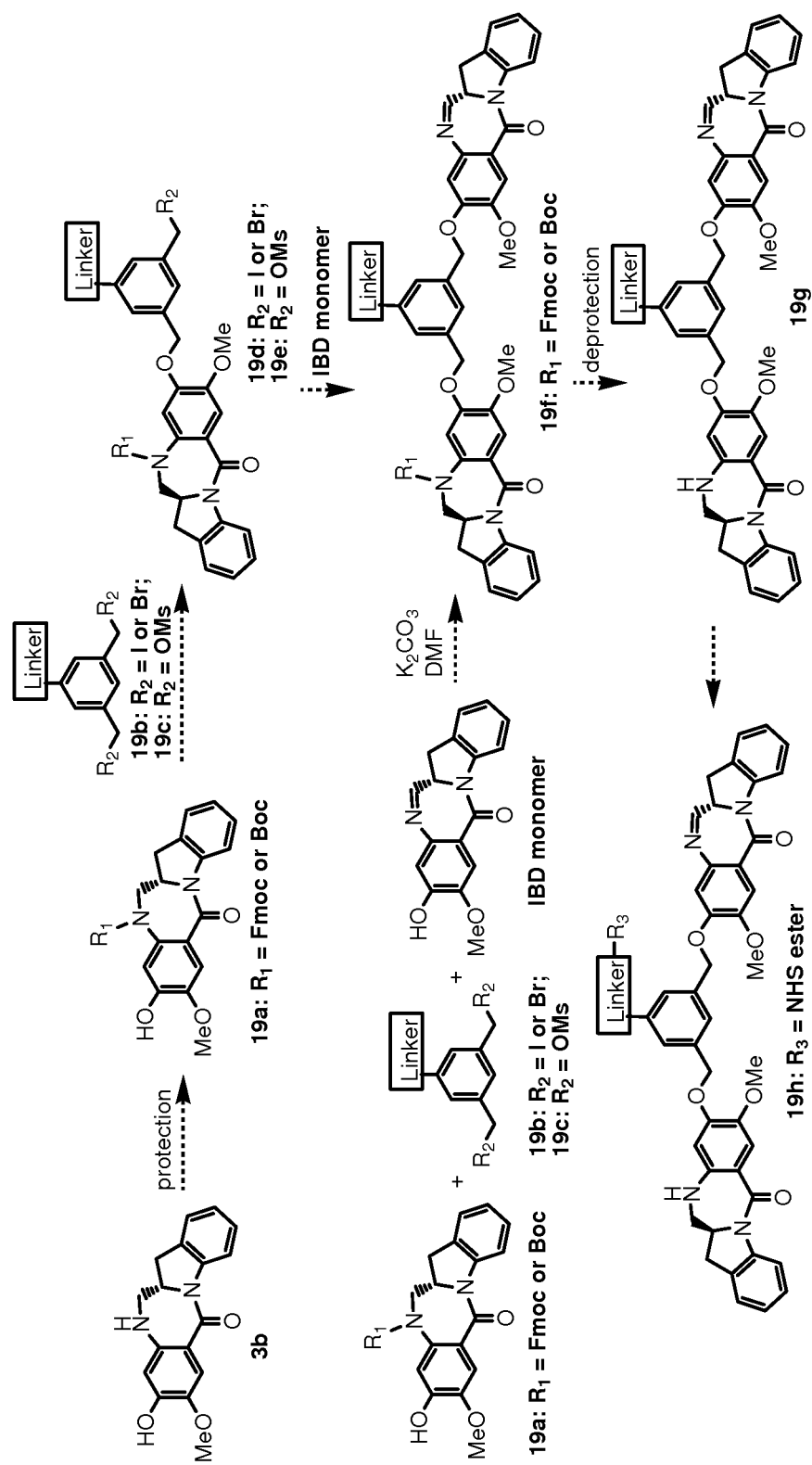


Figure 21. Synthetic Scheme for a Two-step Di-reduced Dimer Synthesis

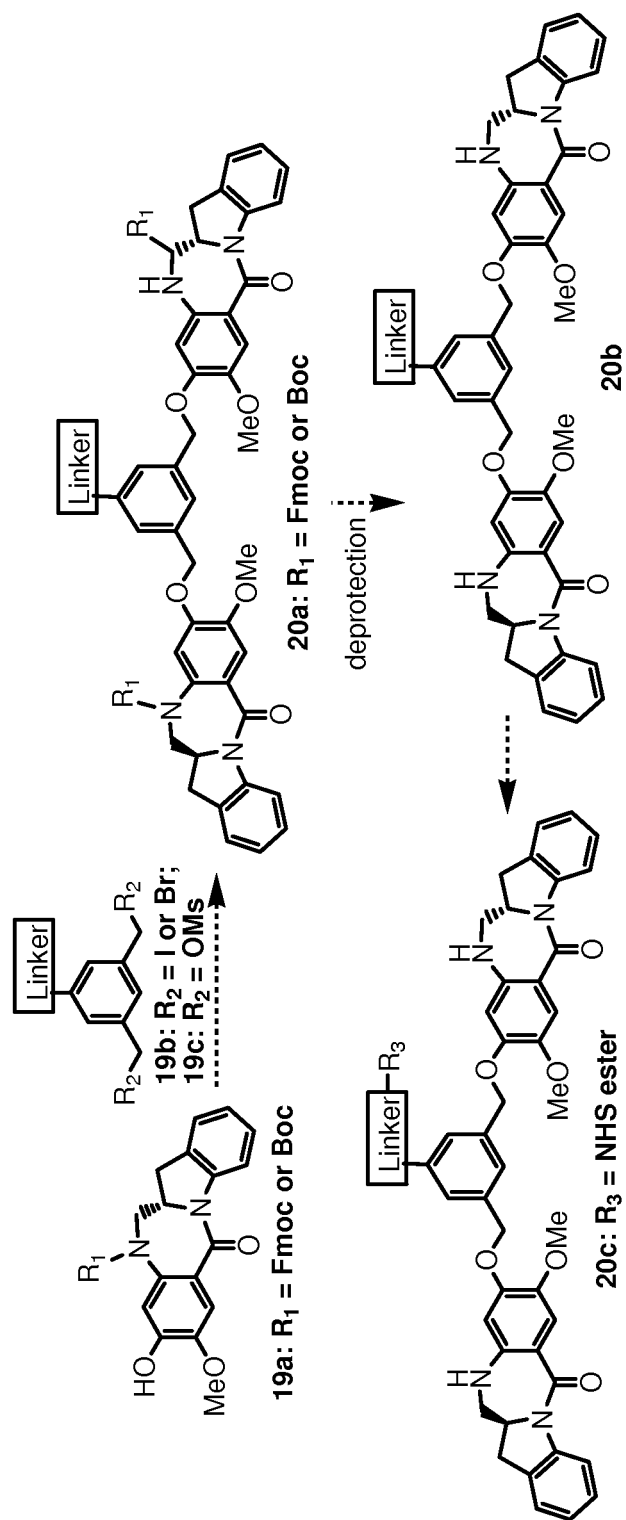
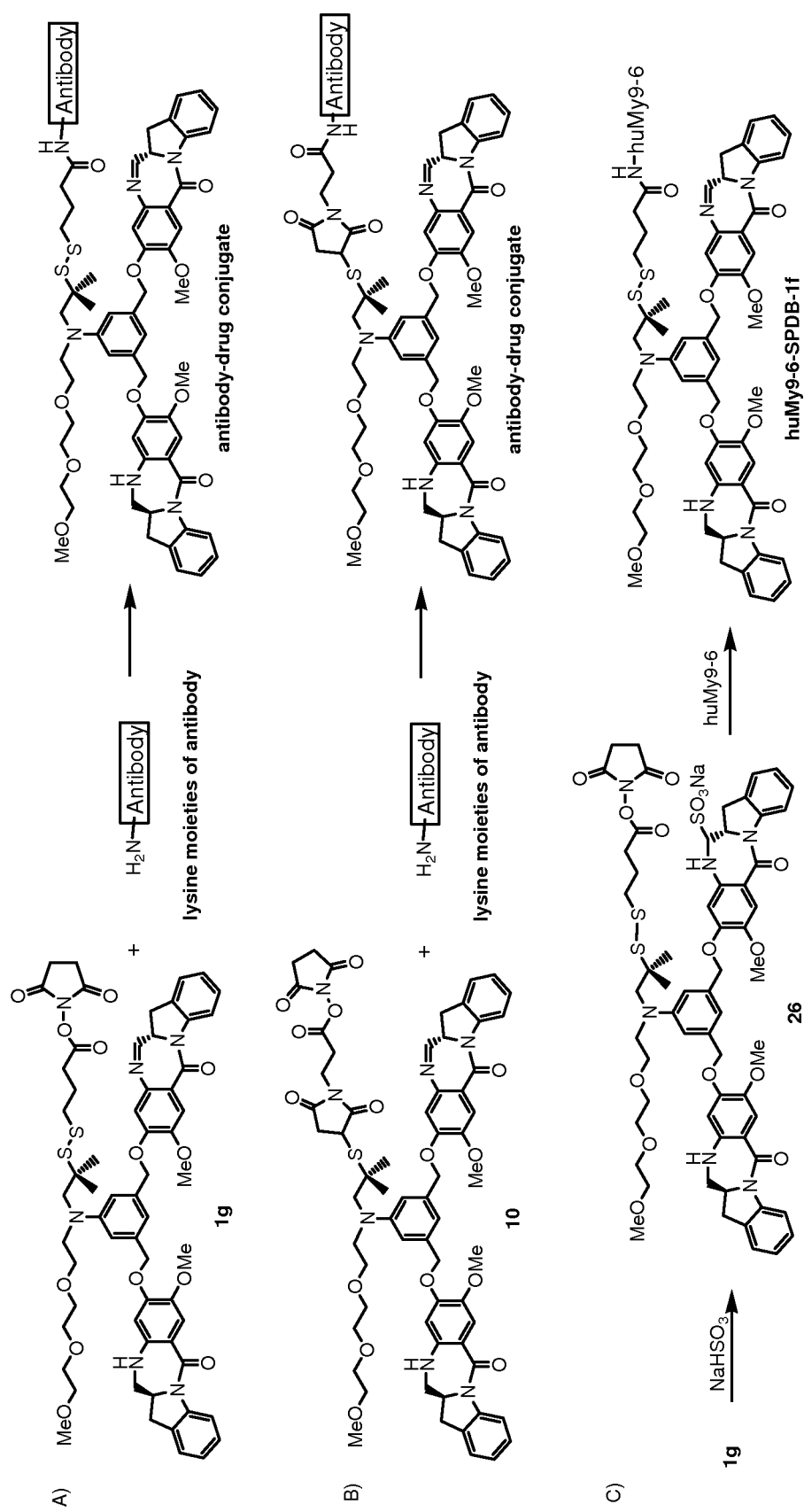


Figure 22. One Step Conjugation Scheme



[illegible]

Representative thiol reactive linkers:

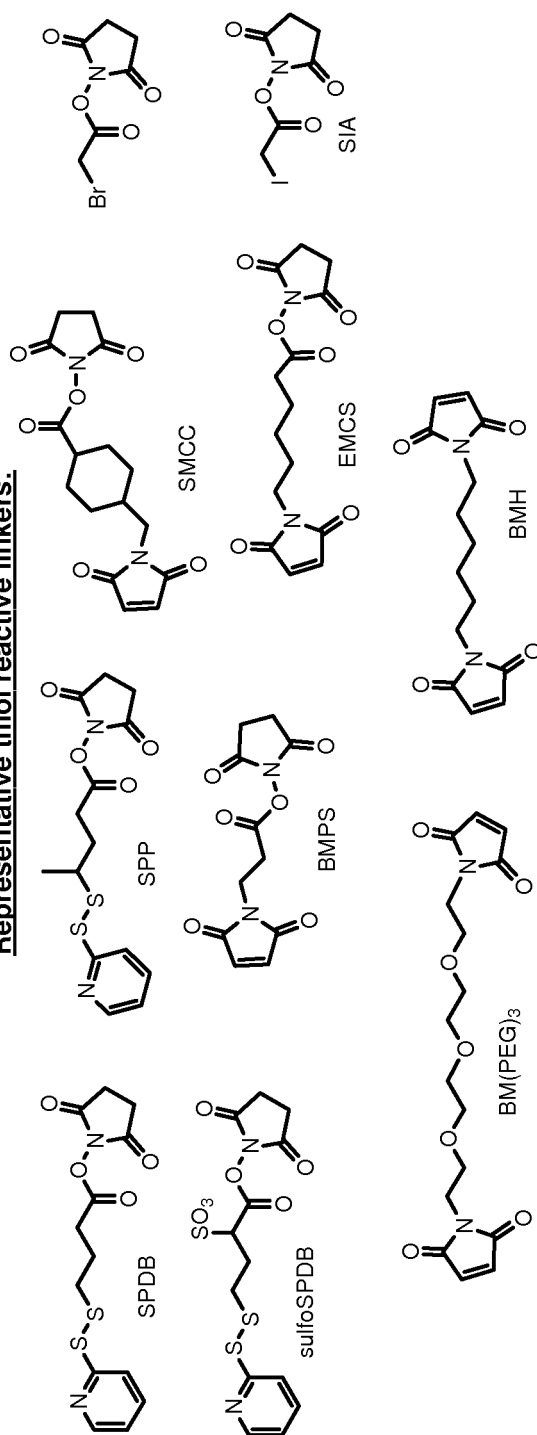


Figure 24. Antiproliferative Activity of Methylthio Dimer **1d** against (A) Namalwa cells, (B) HL60/QC cells, and (C) KB cells

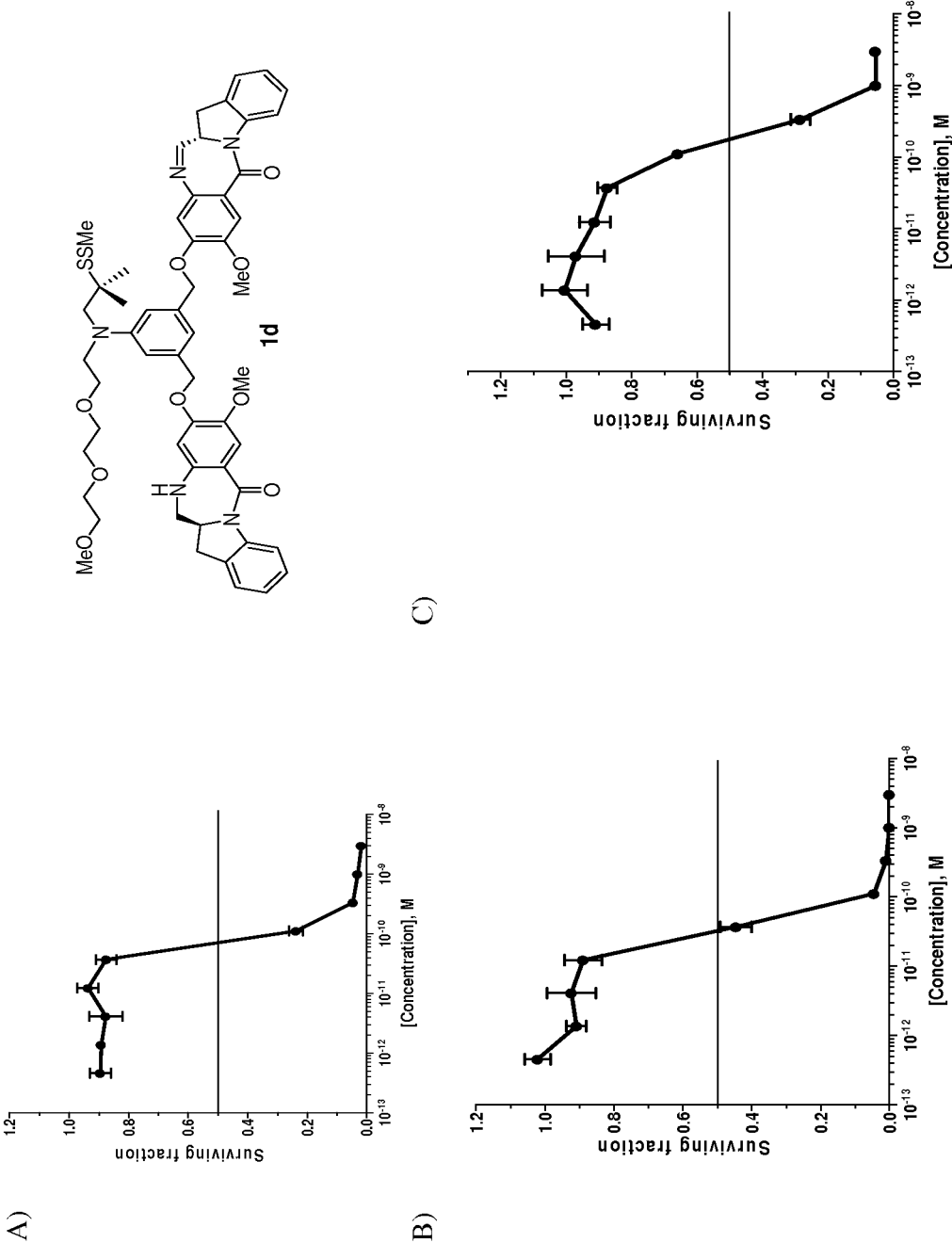


Figure 25. Antiproliferative Activity of huMY9-6-SPDB-1f against (A) HL60/QC (Ag^+) cells with and without blocking of antigen binding sites, (B) HL60/ATCC (Ag^+) cells, and (C) NB-4 (Ag^+) cells

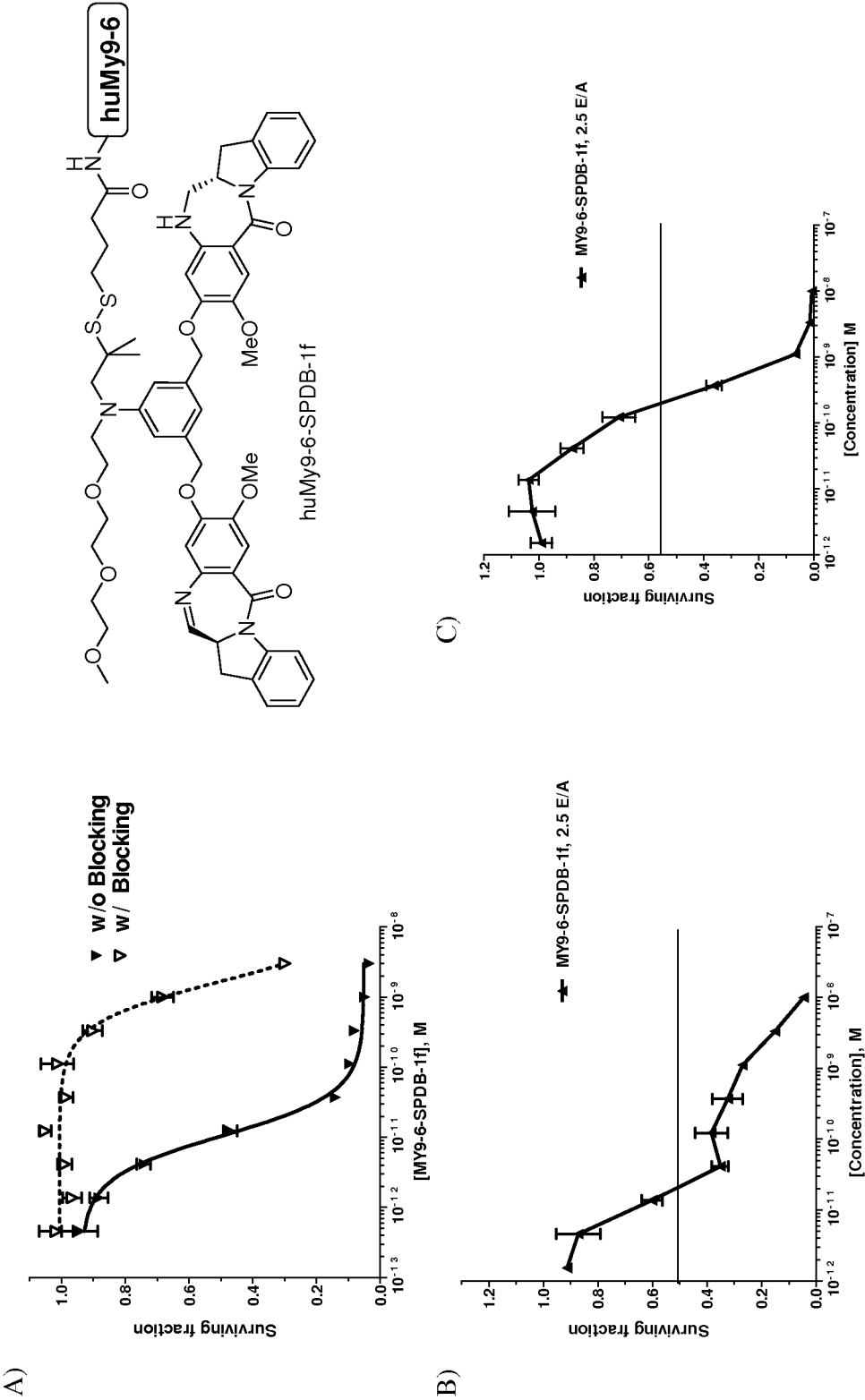


Figure 26. Antiproliferative Activity of huFOLR1-SPDB-1f against KB (Ag⁺) cells with and without blocking of antigen binding sites

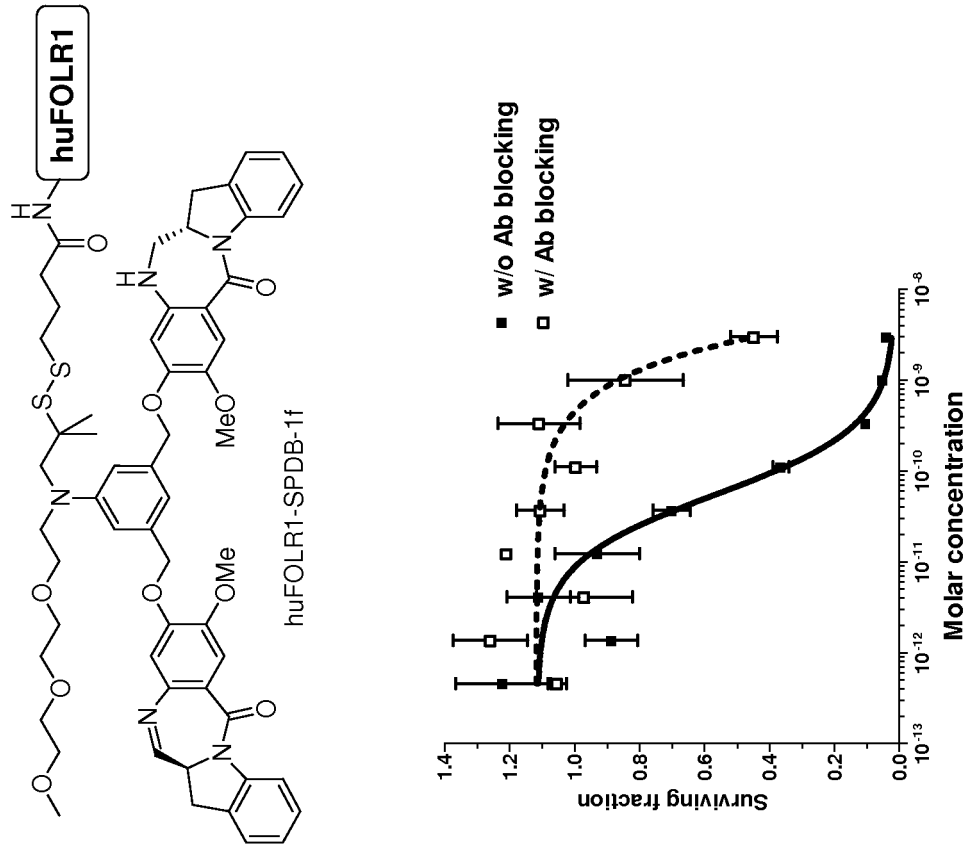


Figure 27. Binding Affinity of huMY9-6-SPDB-1f (FACS analysis)

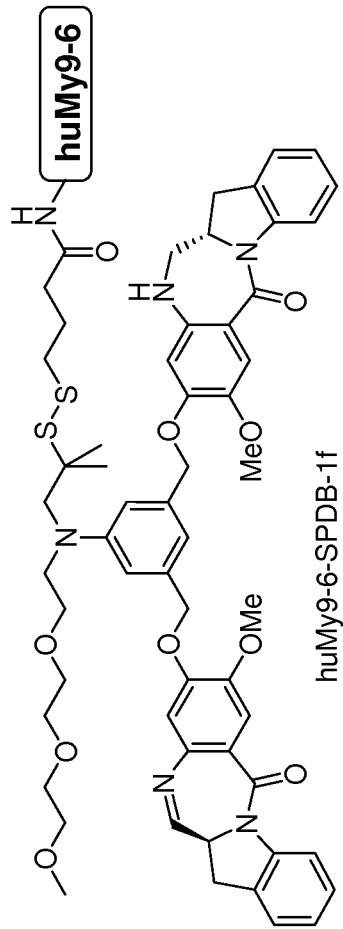
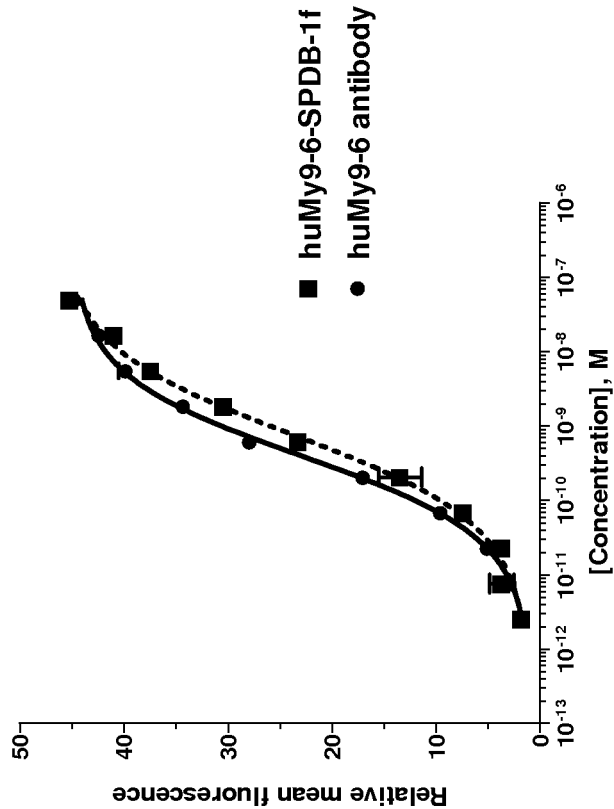


Figure 28. *In vivo* Efficacy of huMy9-6-SPDB-1f in HL60/QC Tumor Bearing Nude Mice

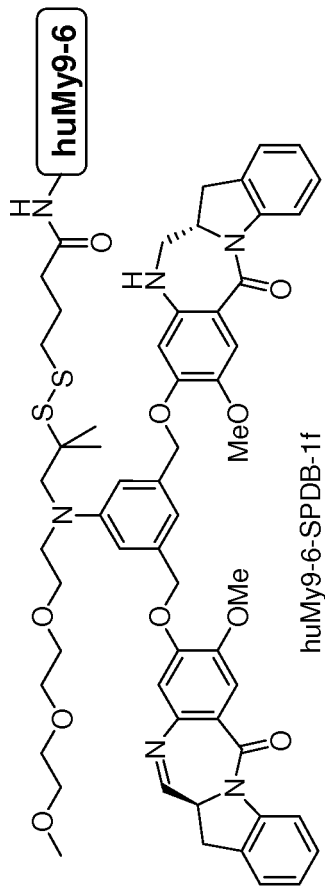
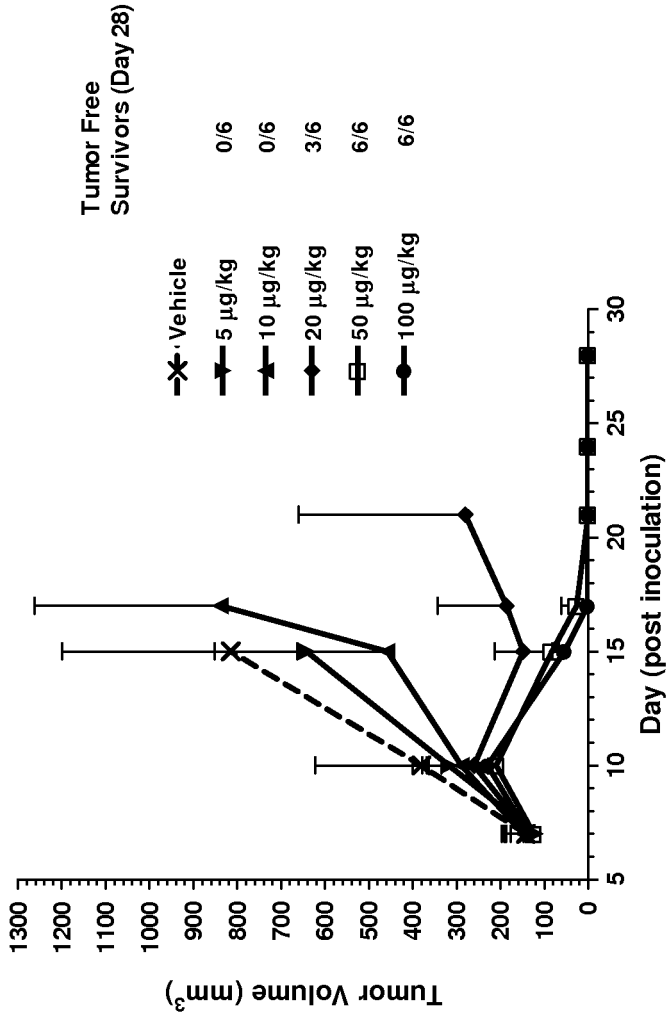


Figure 29. Antiproliferative Activity of huMY9-6-SPDB-1f against Antigen Positive Cell Line (A) HL60/QC cells, (B) HL60/ATCC cells, (C) NB-4 cells, and HEL 92.1.7 cells (D)

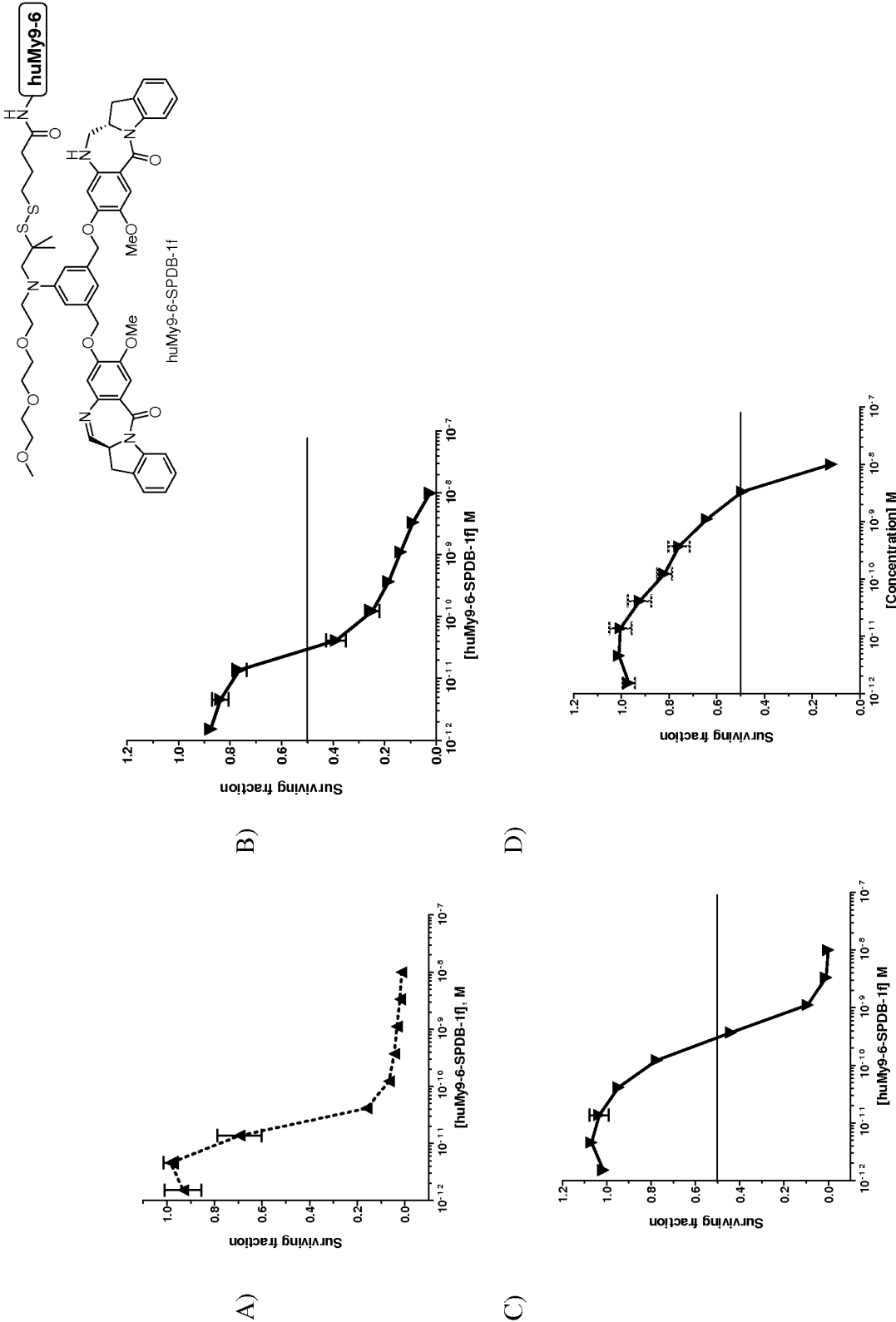


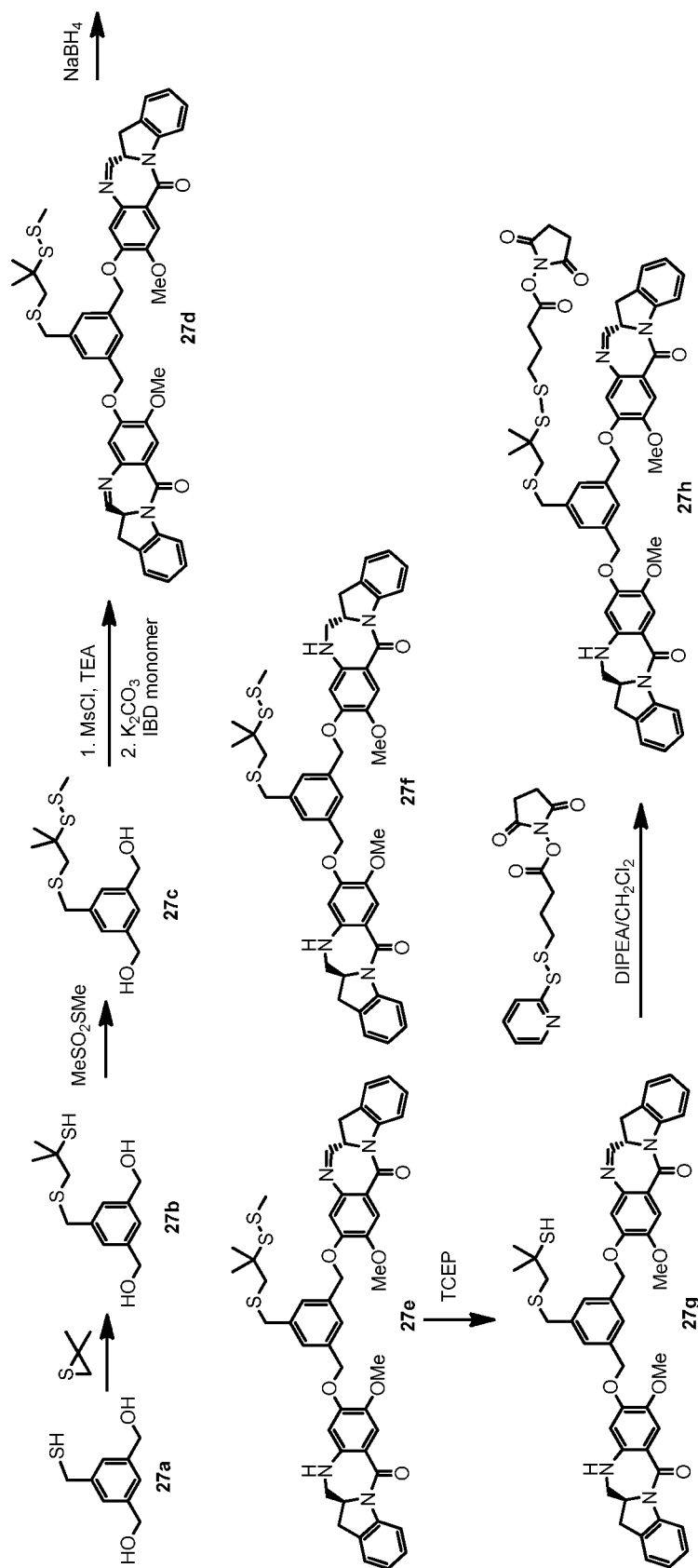
Figure 30. Synthetic Scheme for Thioether-containing Linker Disulfides **27e-h**.

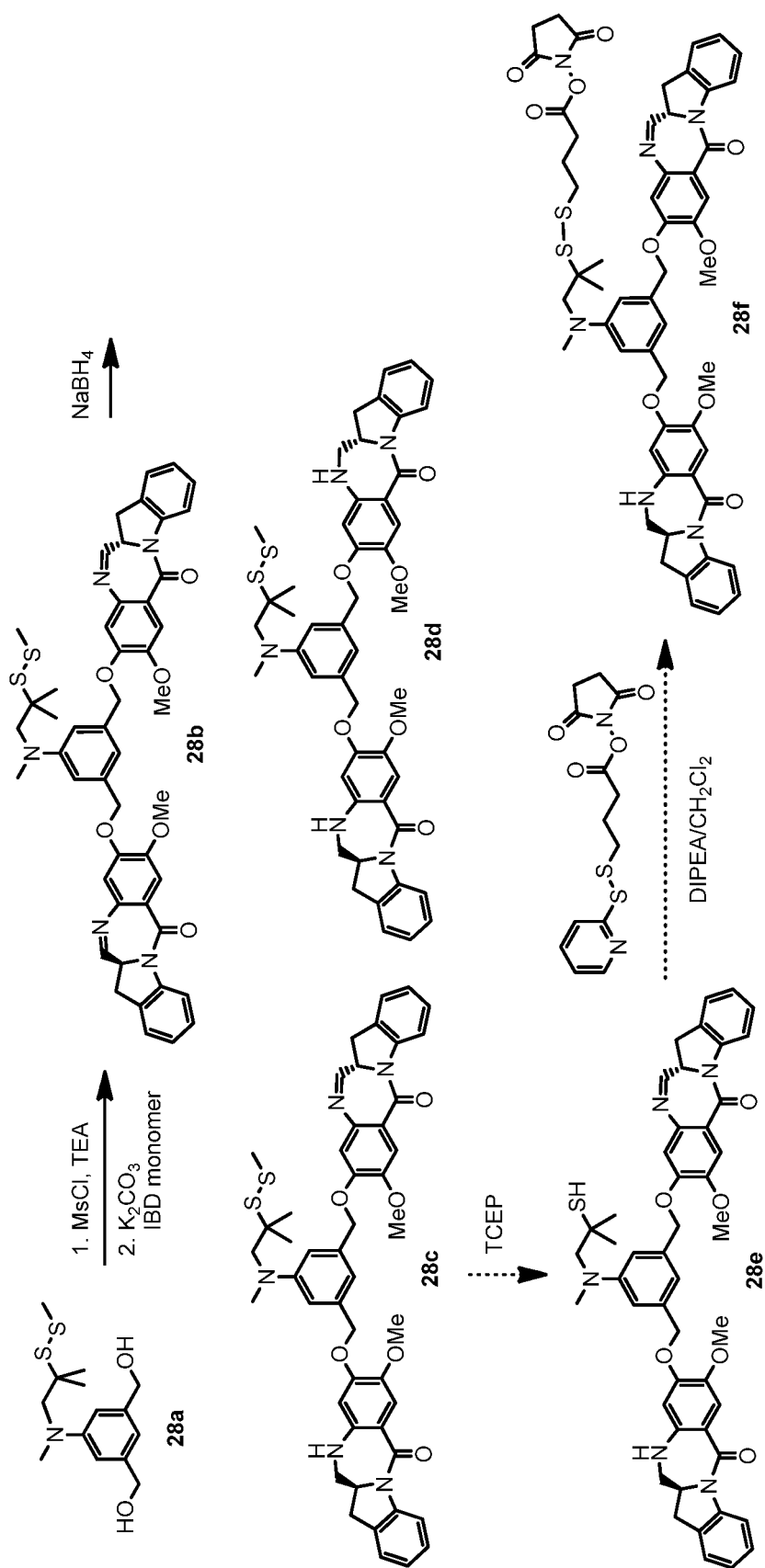
Figure 31. Synthetic Scheme of Dimers **28c-f**

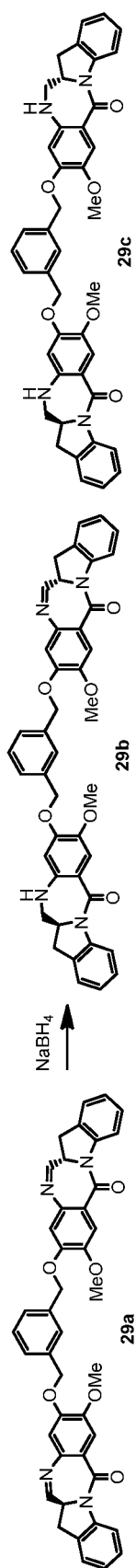
Figure 32. Synthetic Scheme for Phenyl Linked Dimers **29b-c**

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

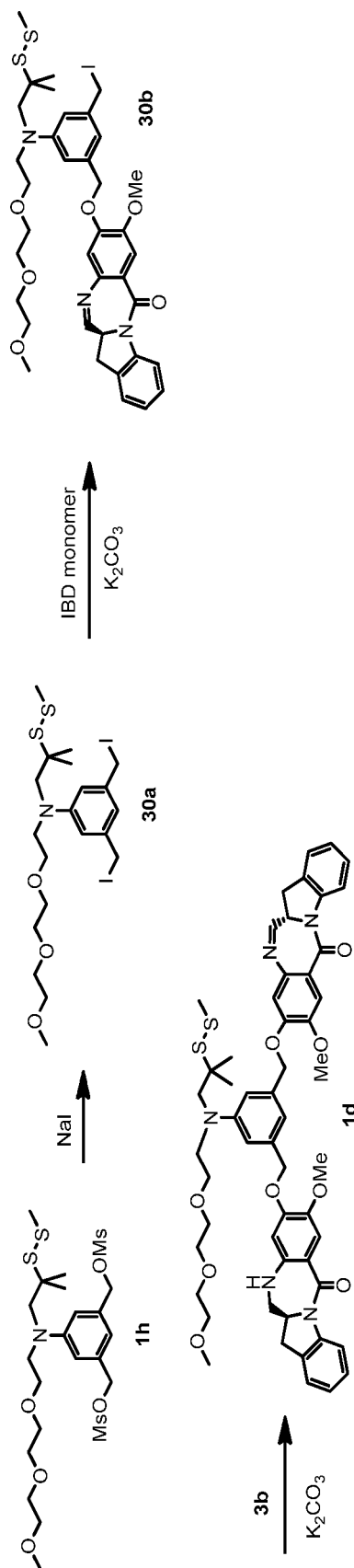


Figure 34. Antiproliferative Activity Comparing (A) huMy9-6-SPDB-1f and (B) huMy9-6-sulfoSPDB-1f, and (C) huMy9-6-BMPS-1f against HL60/QC (Ag^+) Cells with and without Blocking of Antigen Binding Sites

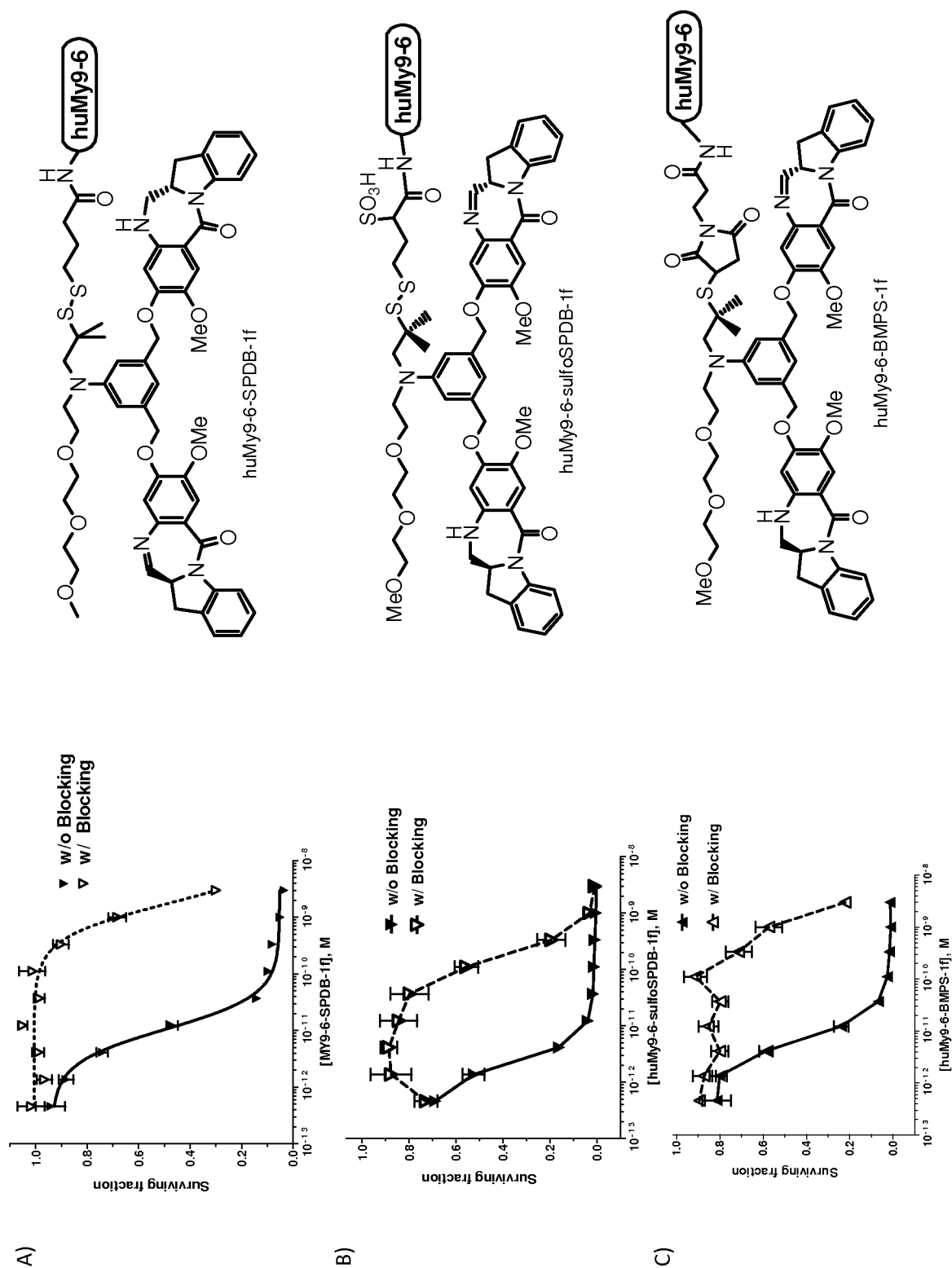


Figure 35. Antiproliferative Activity Comparing (A) chB38.1-SPDB-1f and (B) chB38.1-sulfoSPDB-1f against COLO205 (Ag⁺) cells

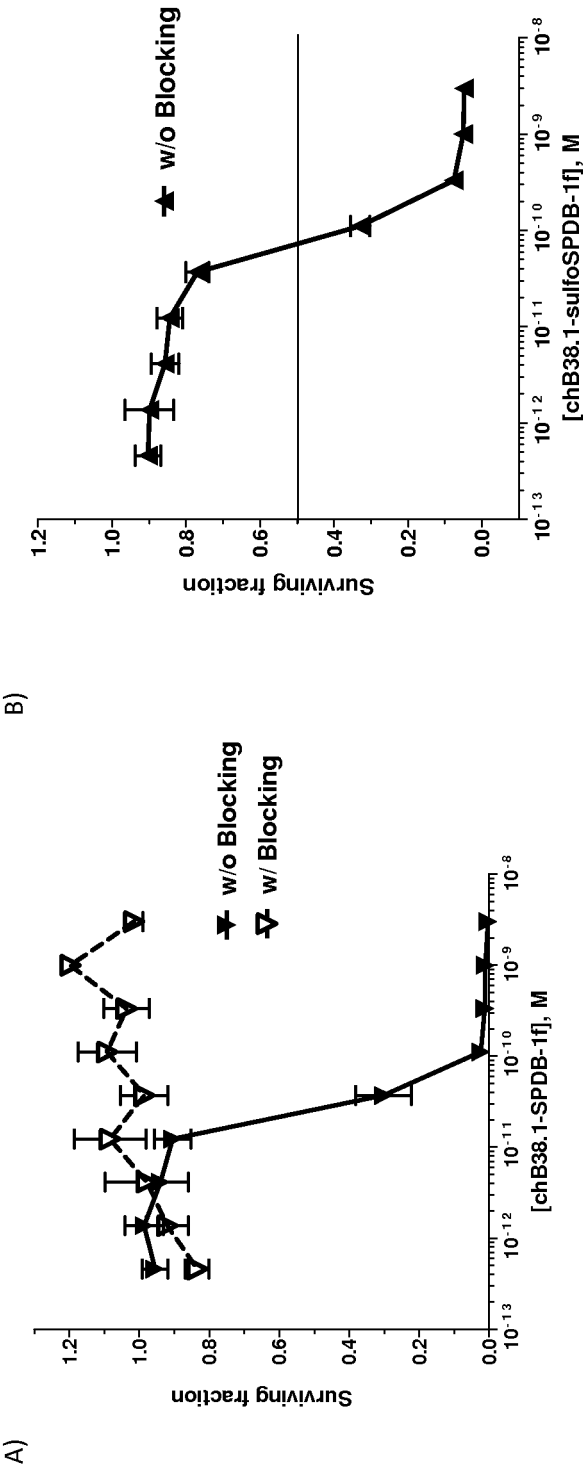


Figure 36. *In vivo* Efficacy of huMy9-6-SPDB-1f in HL60/QC Tumor Bearing Mice

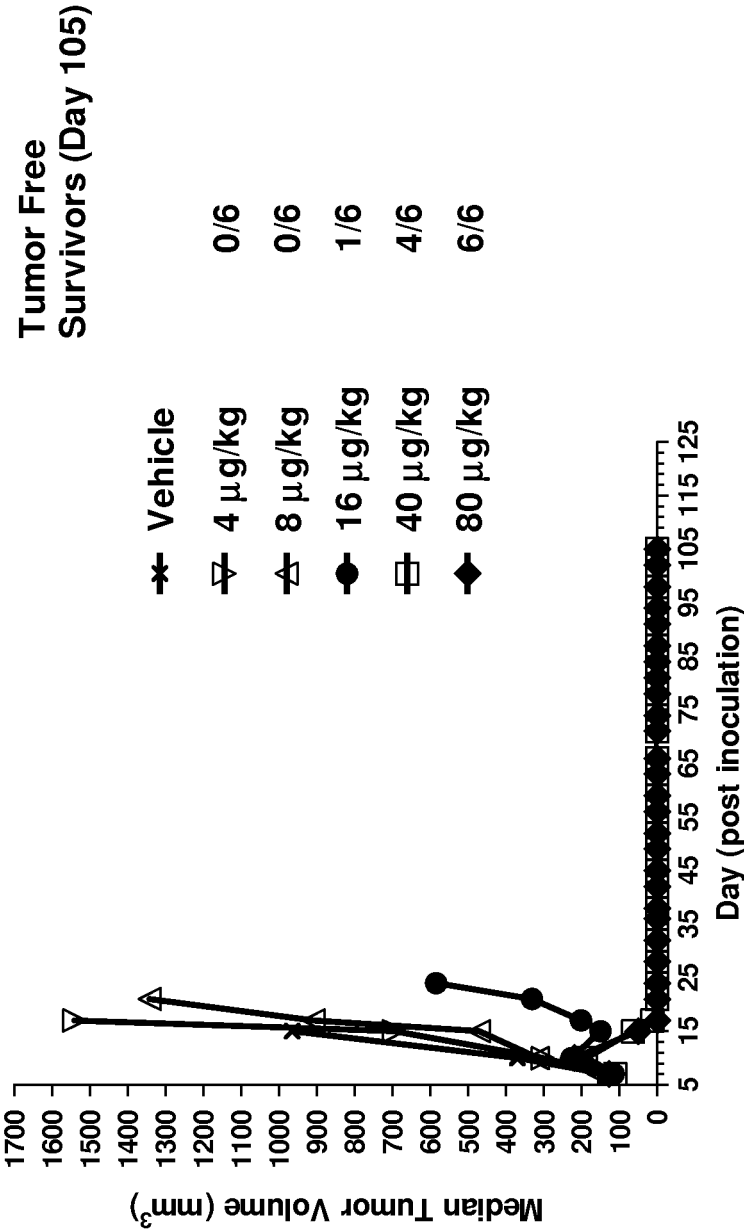


Figure 37. *In vivo* Efficacy of huFOLR1-SPDB-1f in KB Tumor Bearing Mice

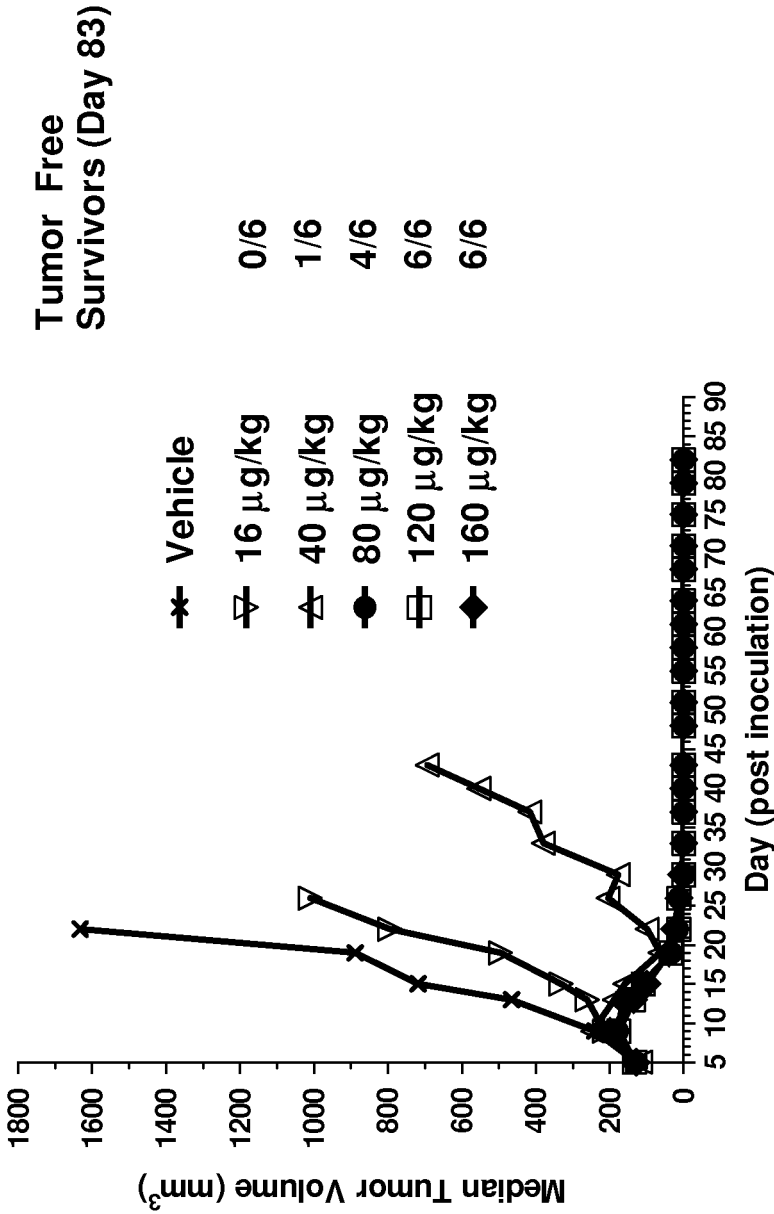


Figure 38. Synthetic Scheme of Compound 1

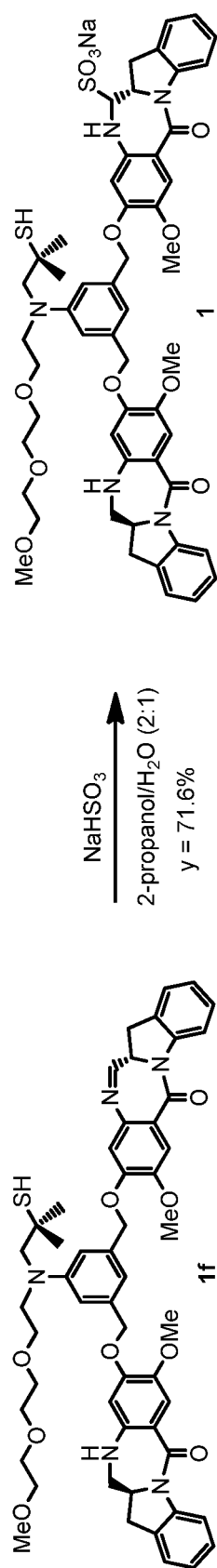


Figure 39. Synthetic Scheme of Compound 1d with 5-ethyl-2-methylpyridine borane (PEMB)

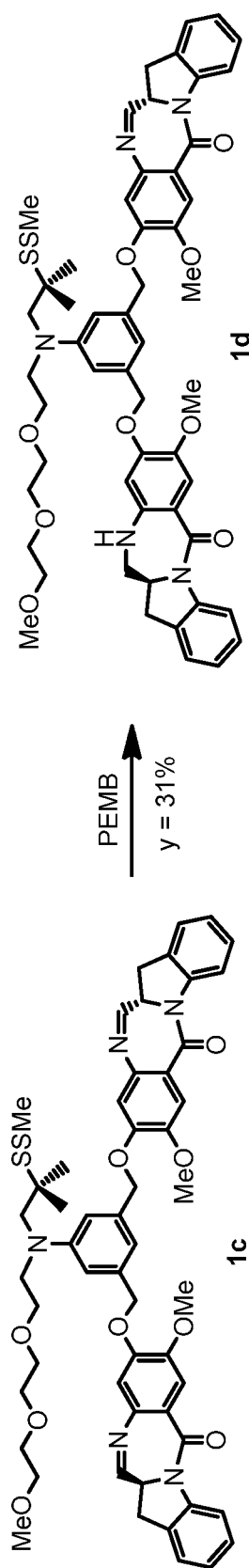


Figure 40. Synthetic Scheme of Compound 1d with sodium triacetoxymethylborohydride (STAB)

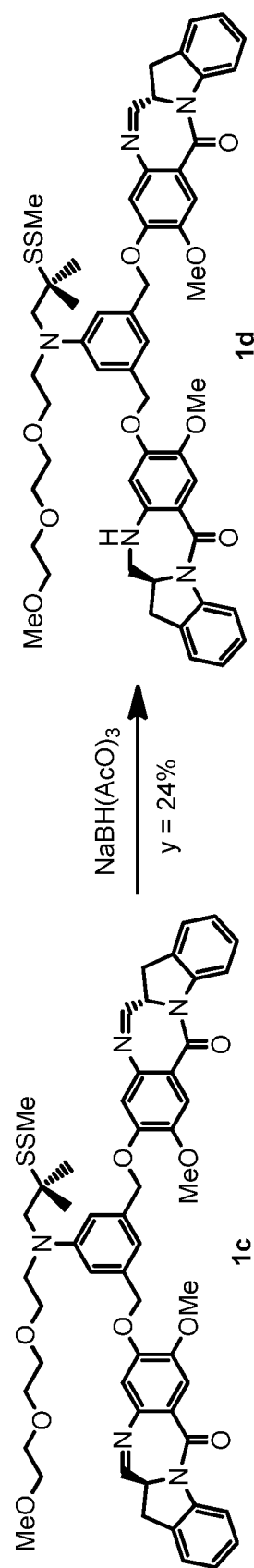


Figure 41. Synthetic Scheme of Compound 31a-c.

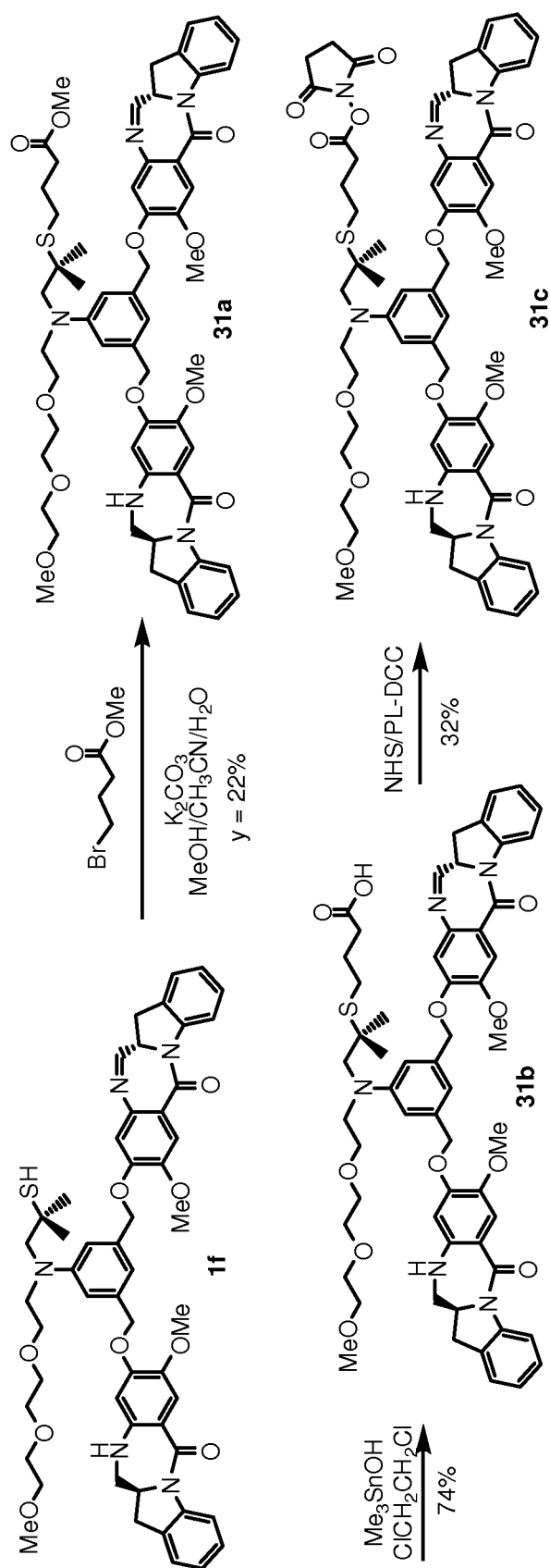


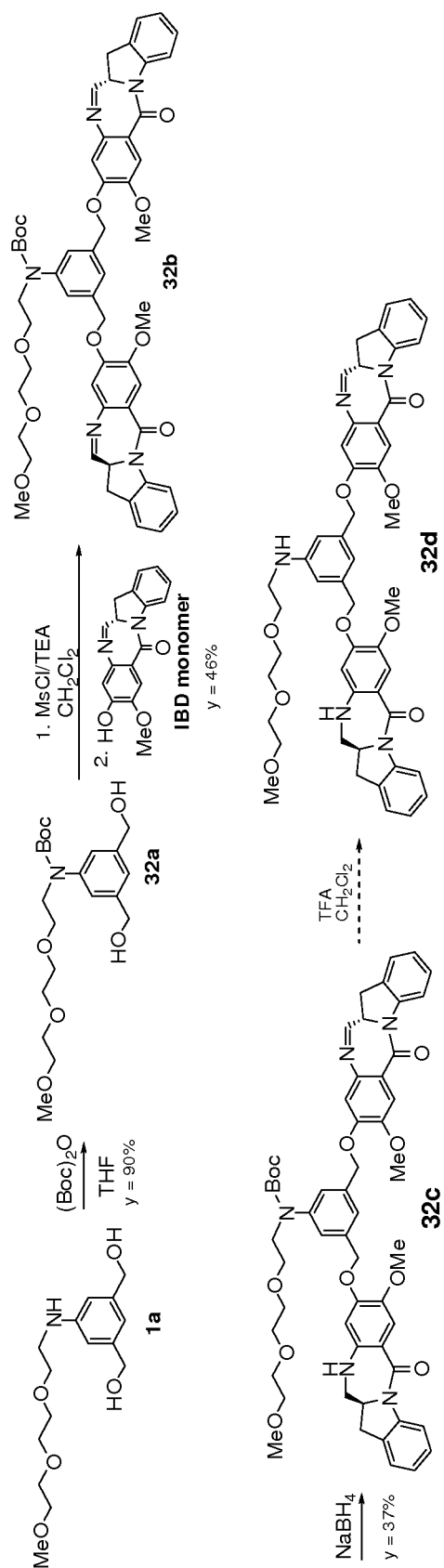
Figure 42. Synthetic Scheme of Compound **32d**

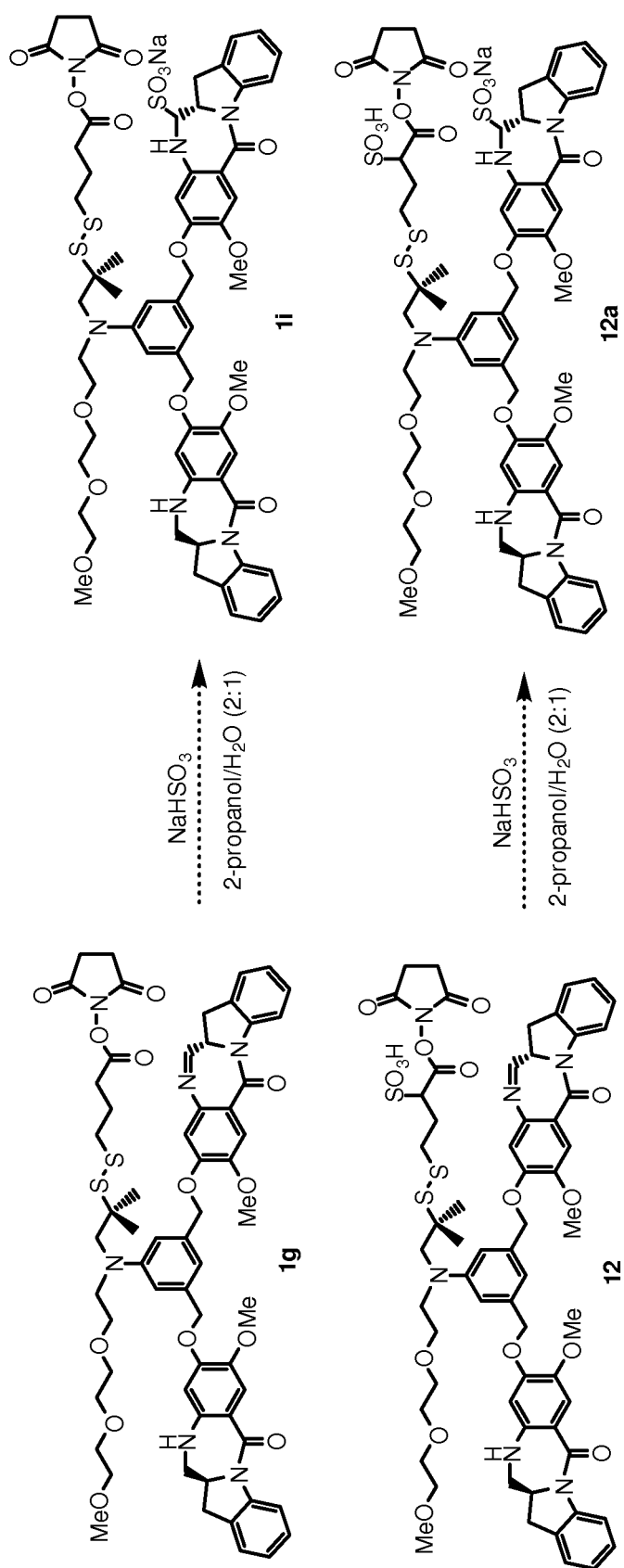
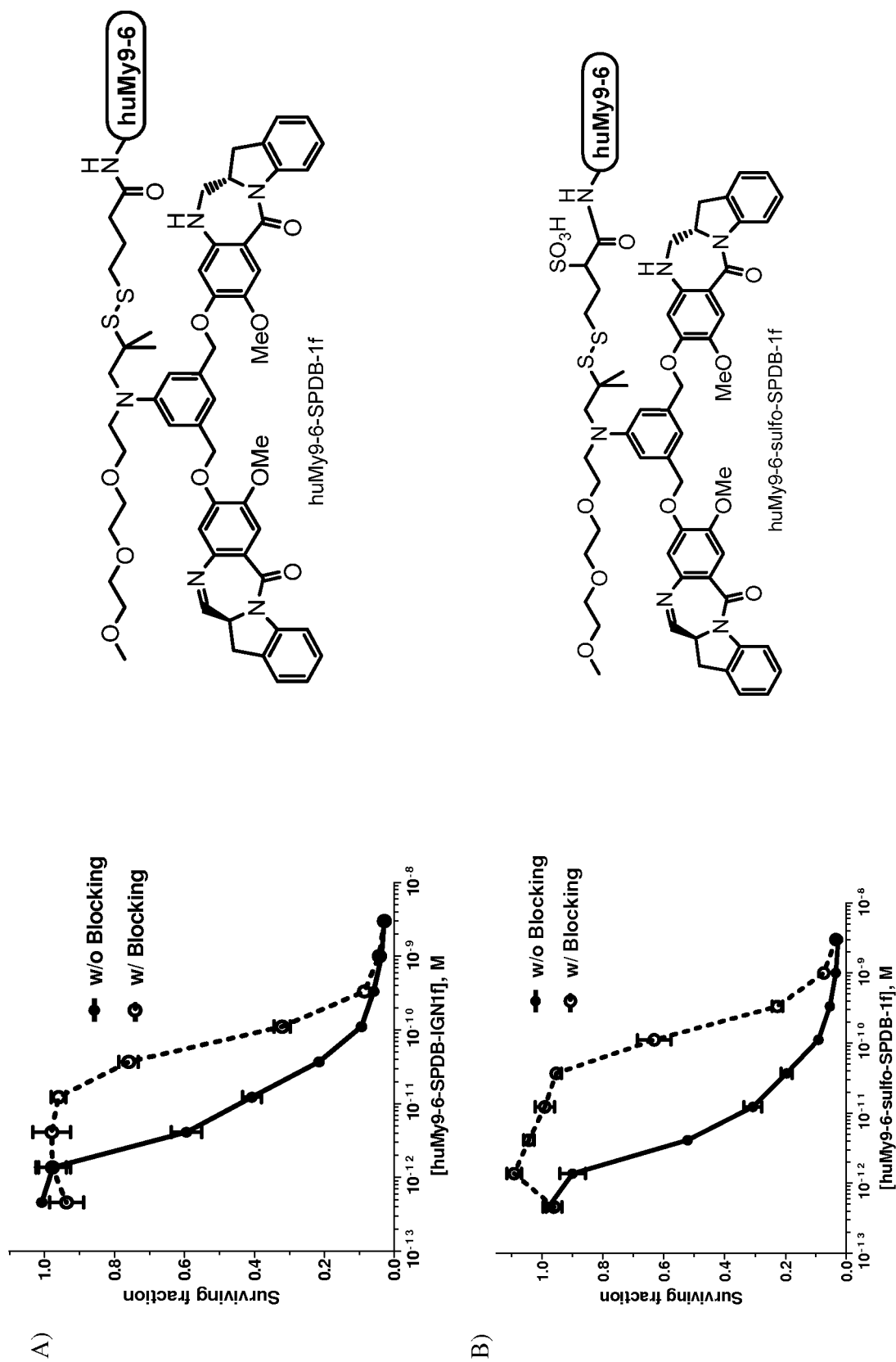
Figure 43. Synthetic Scheme of Compounds **1i** and **12a**

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



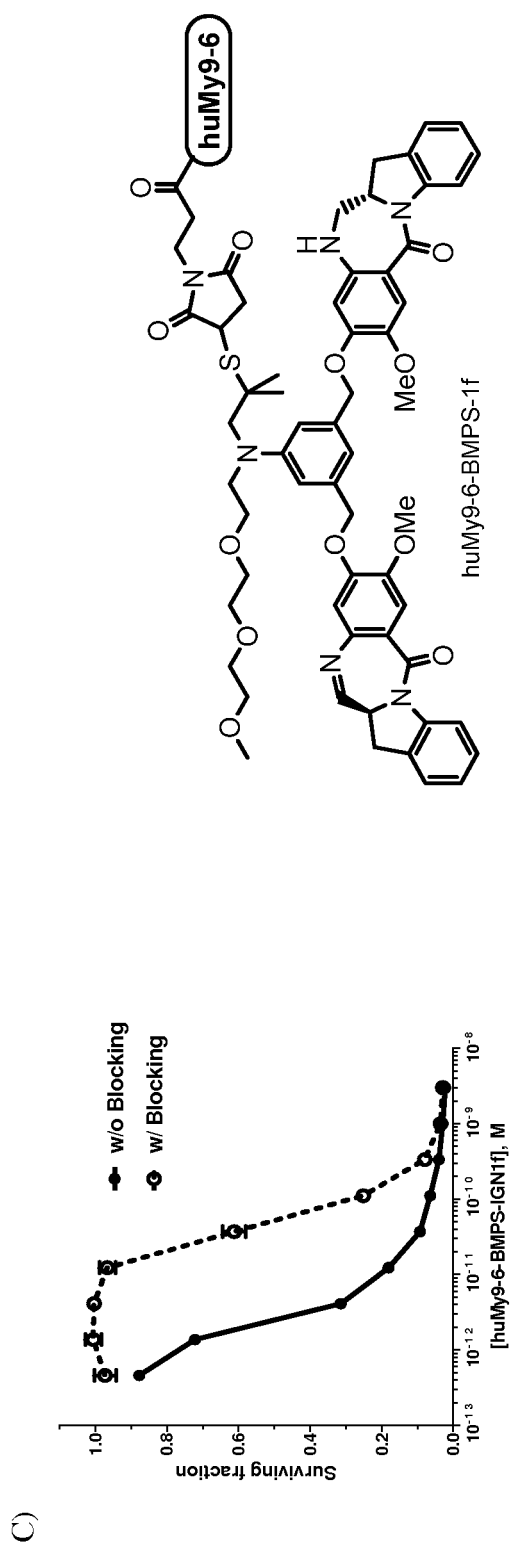


Figure 45. Alternate Synthesis of 4-(benzyloxy)-5-methoxy-2-nitrobenzoic acid used in the Preparation of IBD Monomer

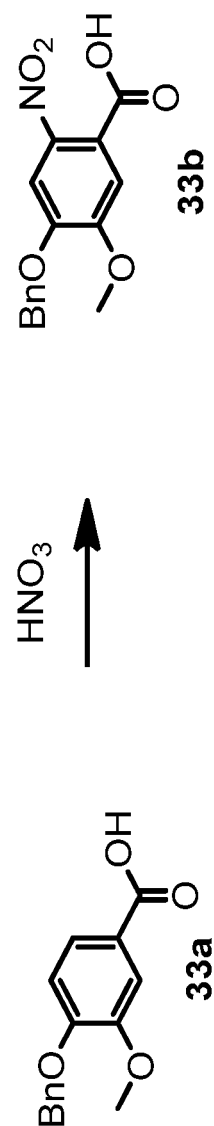


Figure 46. Alternate Synthesis of (5-((2-(2-methoxyethoxy)ethoxy)ethyl)(2-methyl-2-(methyldisulfanyl)propyl)amino)-1,3-phenylene)dimethanol (**1b**)

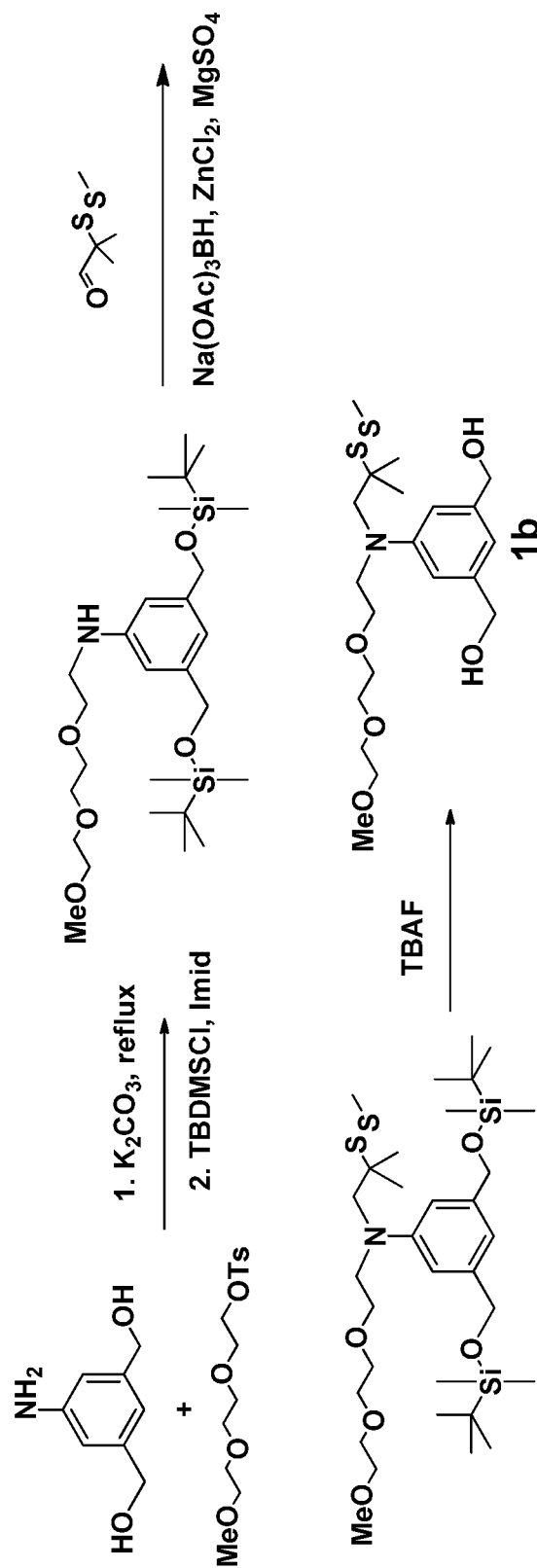


Figure 47. Alternate Synthesis of (5-((2-(2-methoxyethoxy)ethoxy)ethyl)(2-methyl-2-(methyldisulfanyl)propyl)amino)-1,3-phenylene)dimethanol (**1b**)

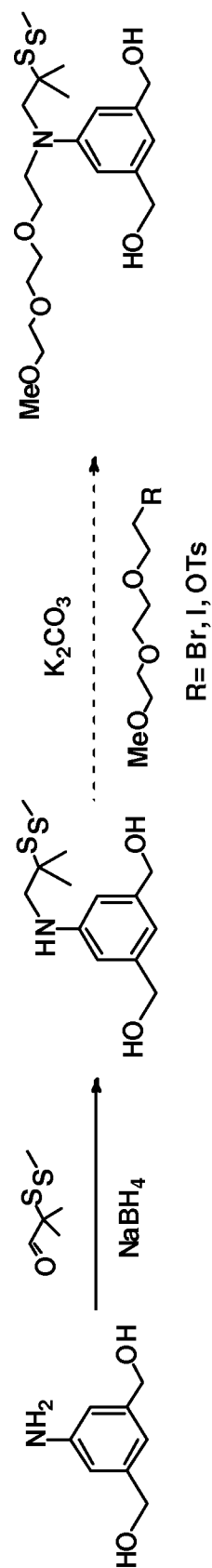


Figure 48. Alternate Synthetic Scheme for a Two-step Mono-imine Dimer Synthesis

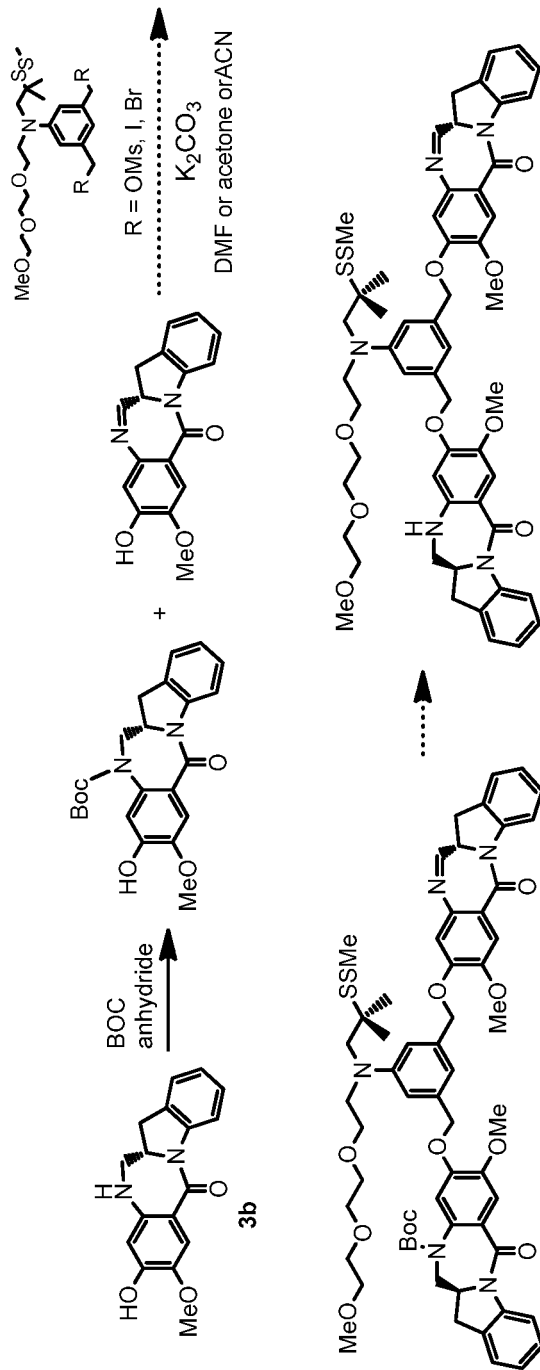


Figure 49. Potency of Conjugates against Various Cell Lines Measured by IC_{50} values (nM)

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

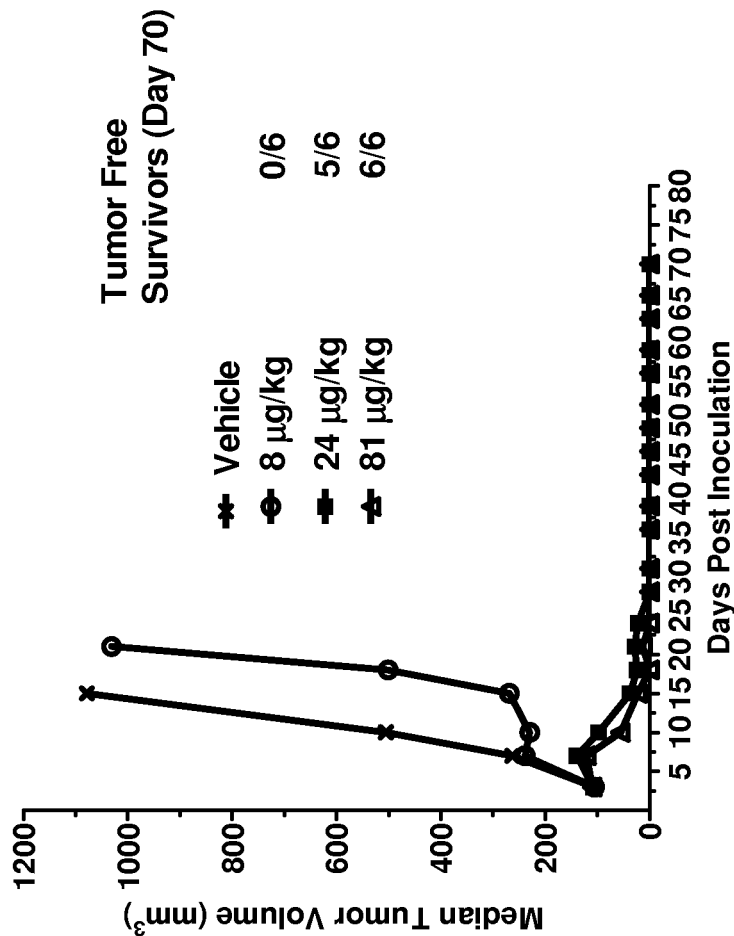


Figure 51. *In Vivo* Efficacy of huMy9-6-sulfo-SPDB-1f in NB4 Tumor Bearing Mice

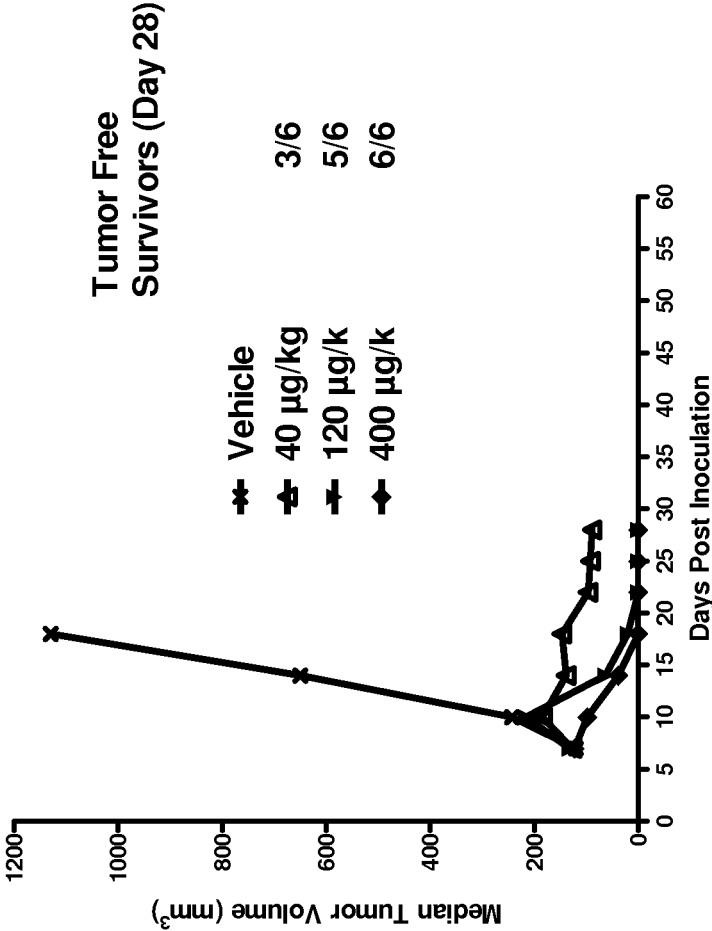


Figure 52. *In Vivo* Efficacy of huMy9-6-BMPS-1f in HL60/QC Tumor Bearing Mice

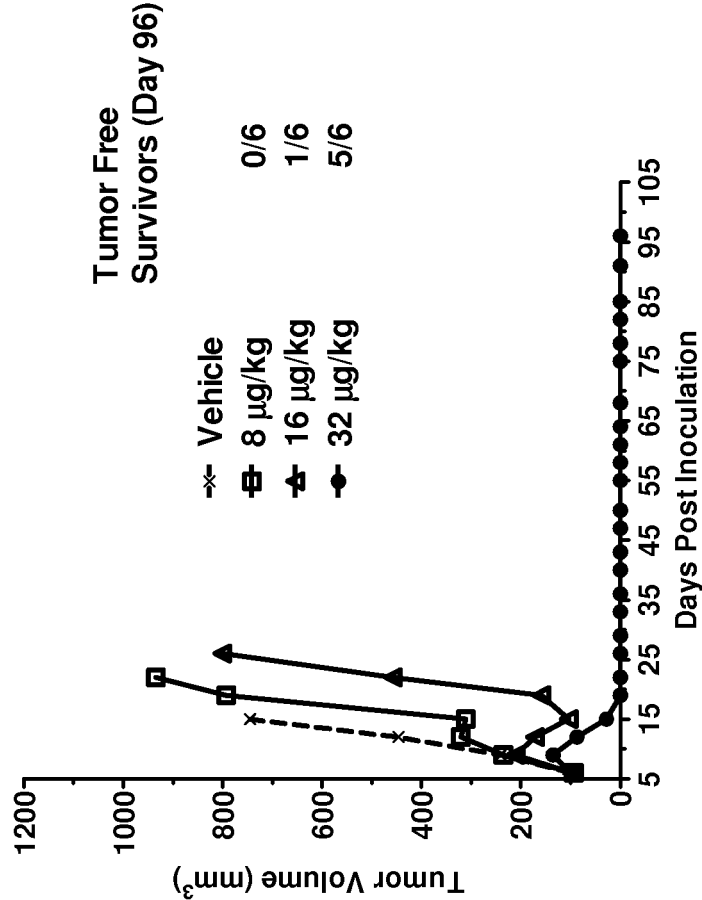


Figure 53. *In vivo* Efficacy of huMy9-6-BMPS-1f in MOLM-13 Tumor Bearing Mice

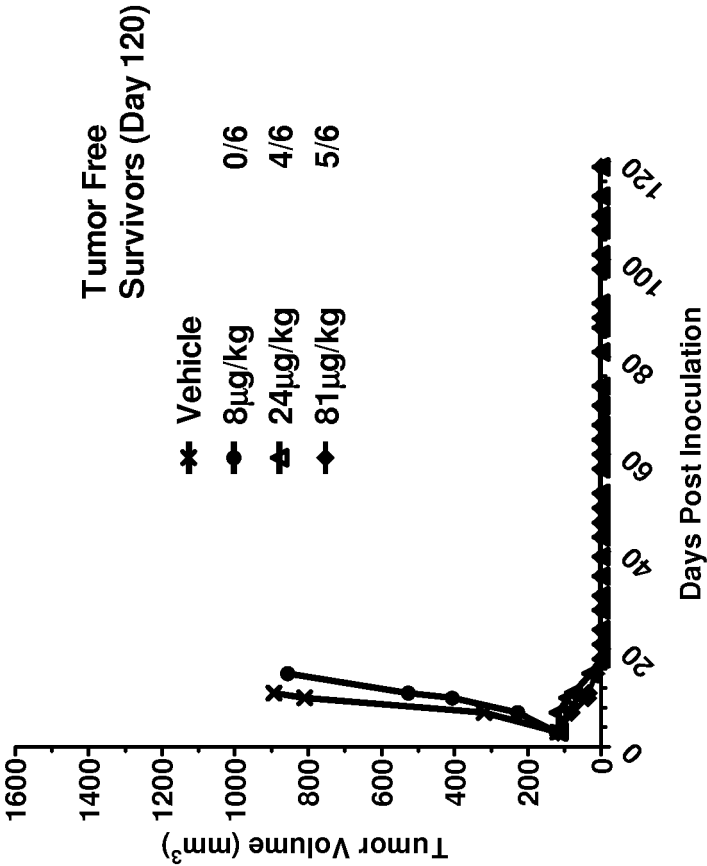


Figure 54. Representative Synthesis Scheme for a Sulfonated Folate / Cytotoxic Compound Conjugate

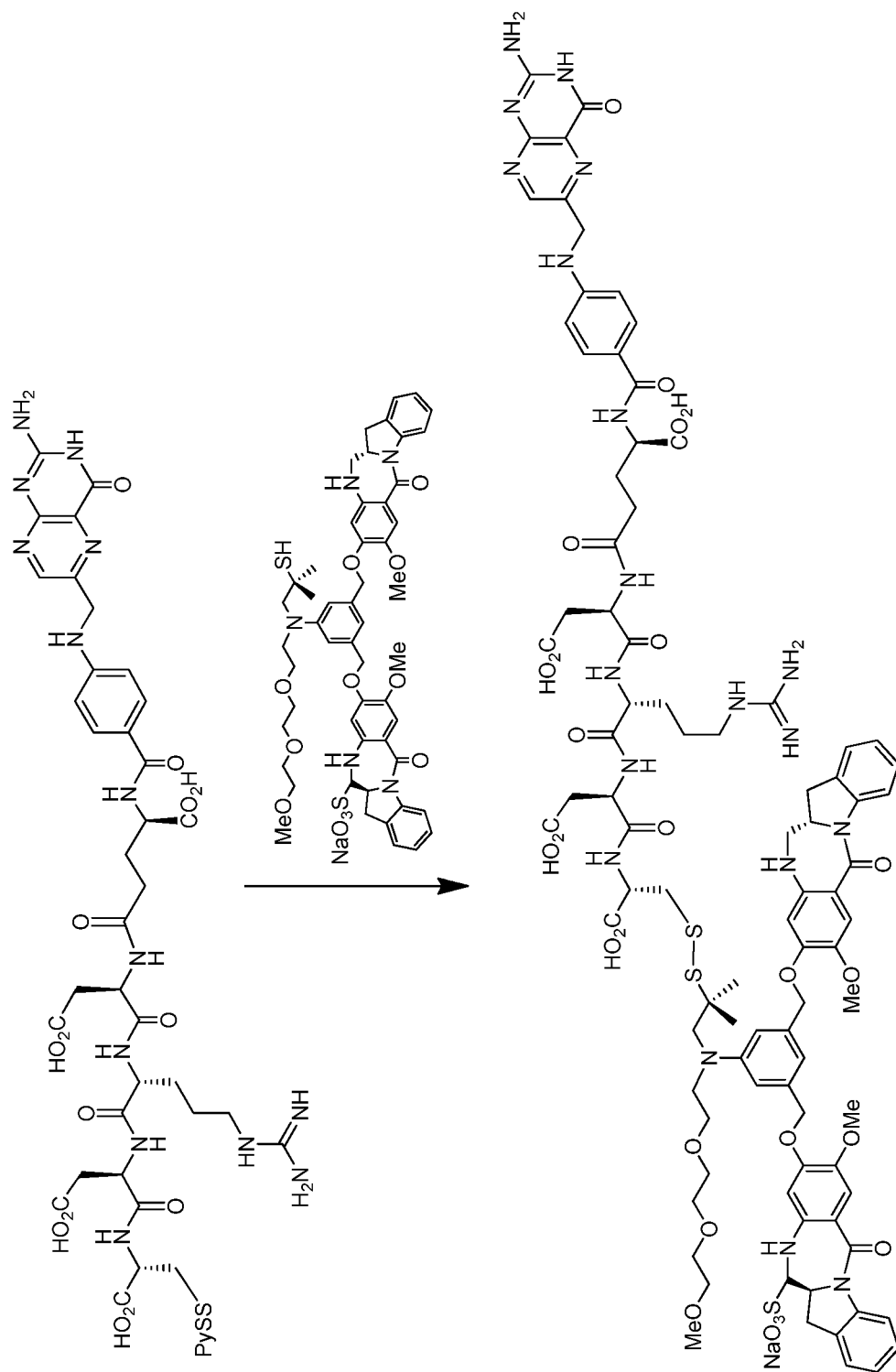


Figure 55. Structures of Several Sulfonated Drug-Antibody (huMy9-6) Conjugates

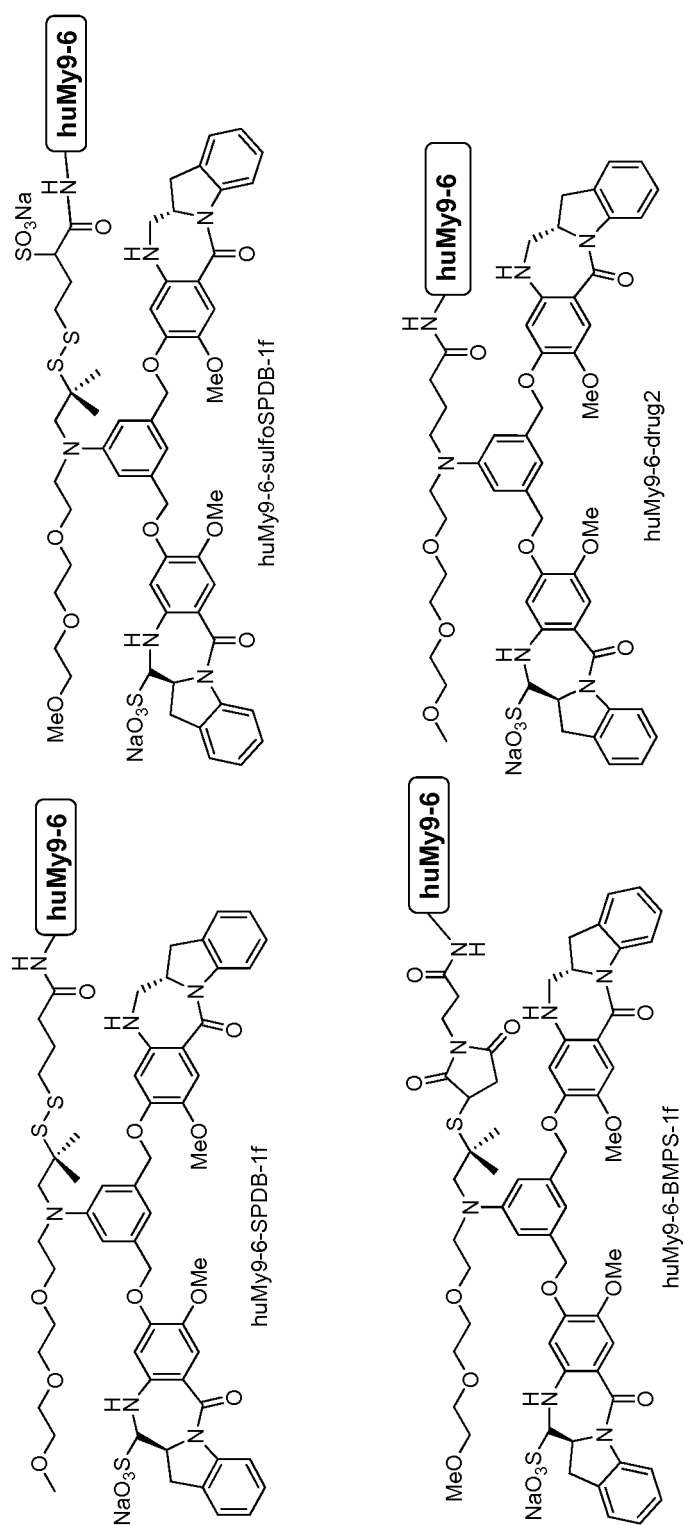


Figure 56. *In vivo* Efficacy of huMy9-6-drug2 in HL60/QC Tumor Bearing Mice

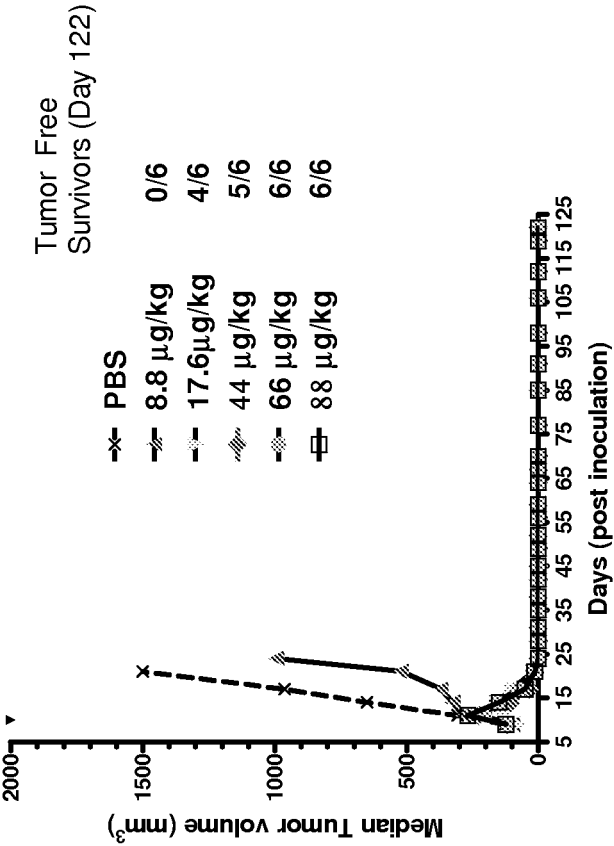
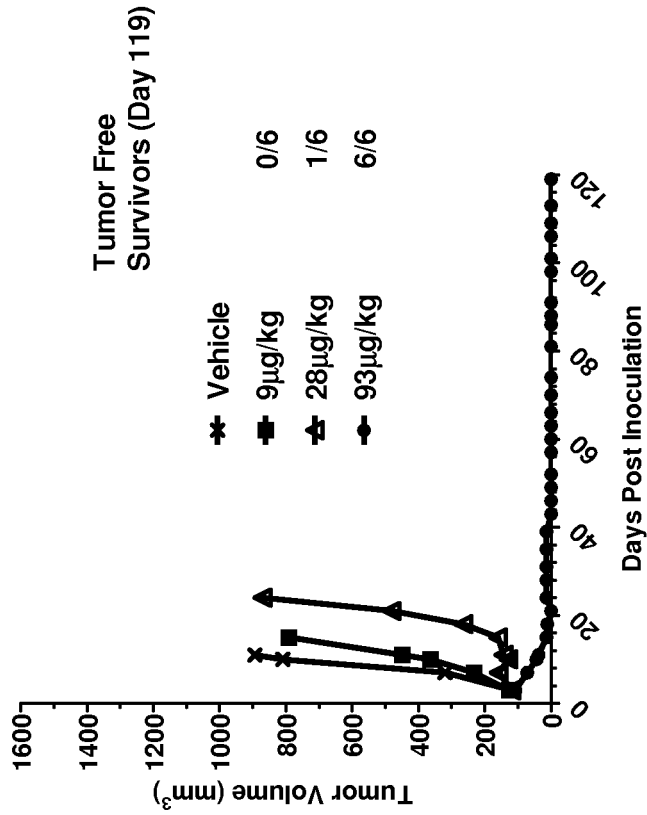


Figure 57. *In vivo* Efficacy of huMy9-6-drug2 in MOLM-13 Tumor Bearing Mice



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

Figure 58.

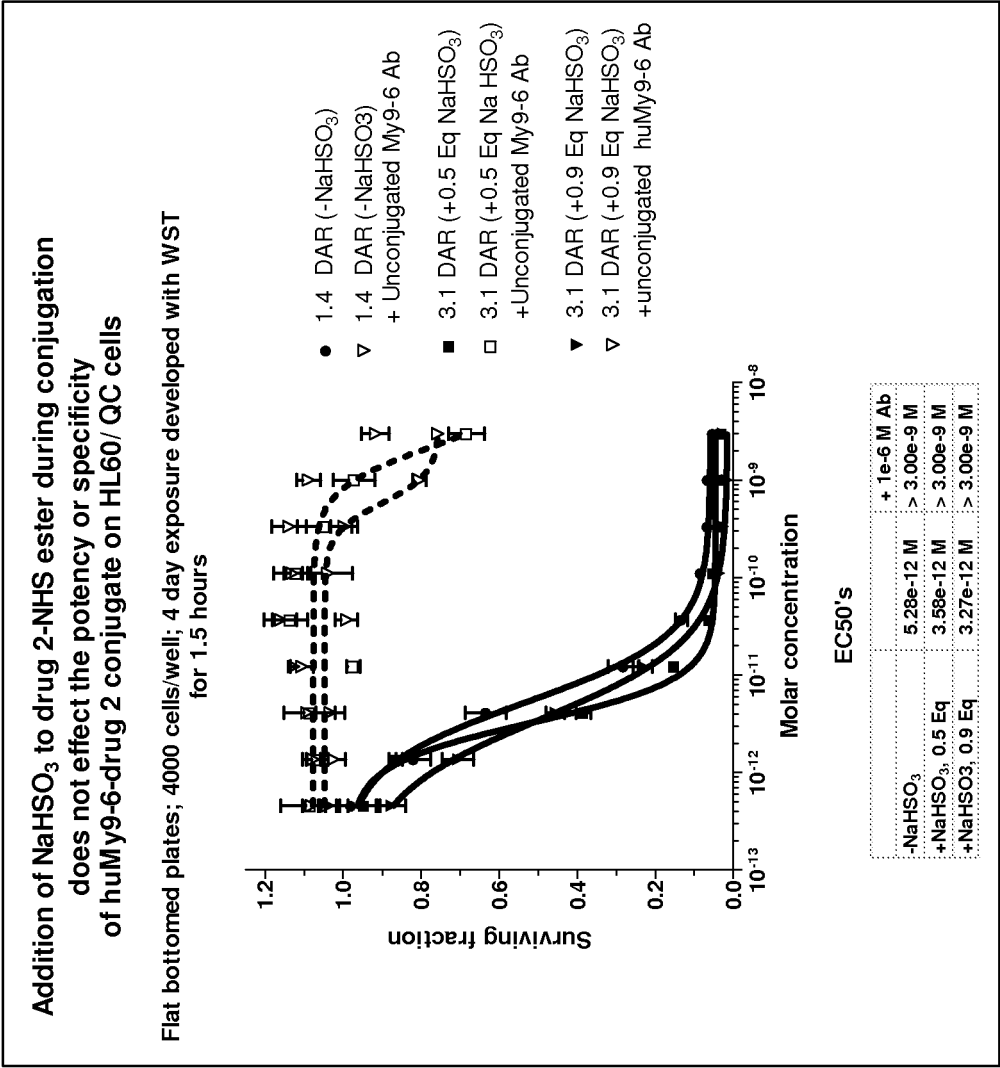


Figure 59.

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

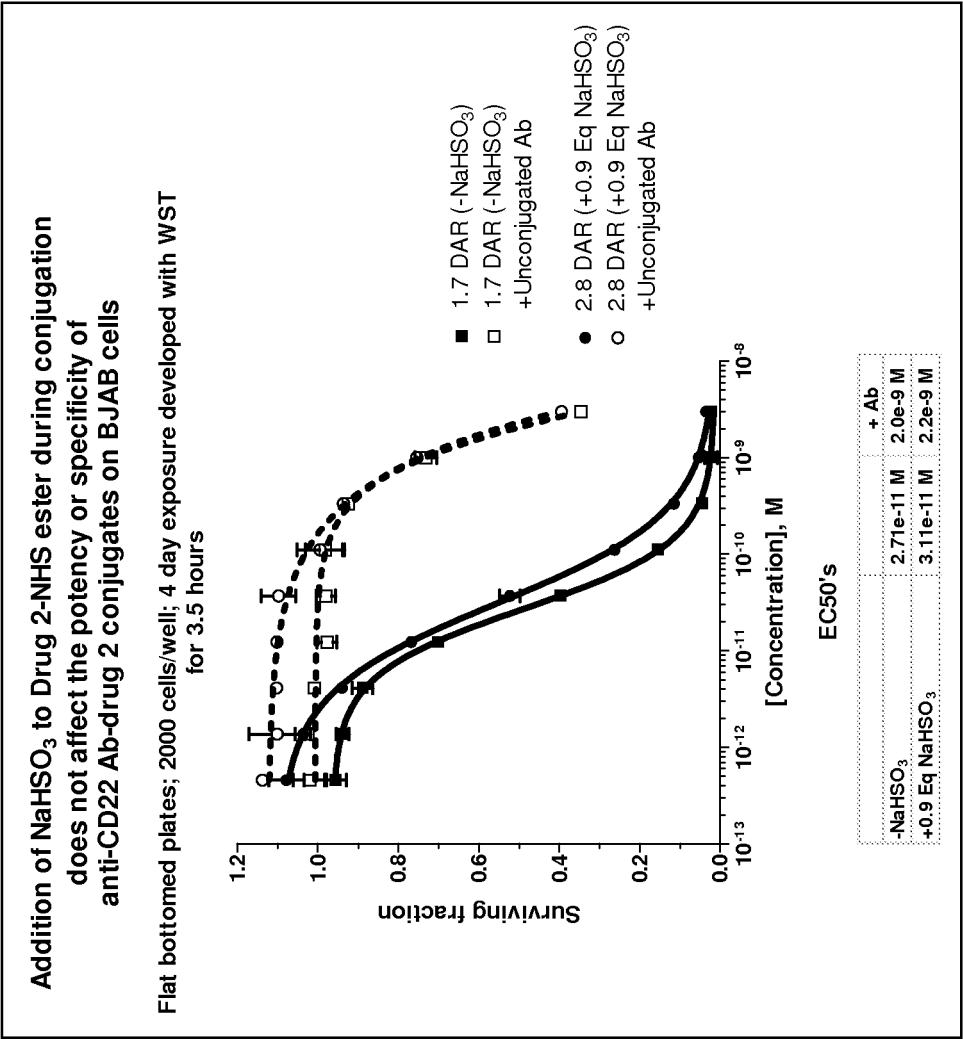


Figure 60.

