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Tetrahedron Prize for Creativity in Organic Chemistry 2005 B. Giese

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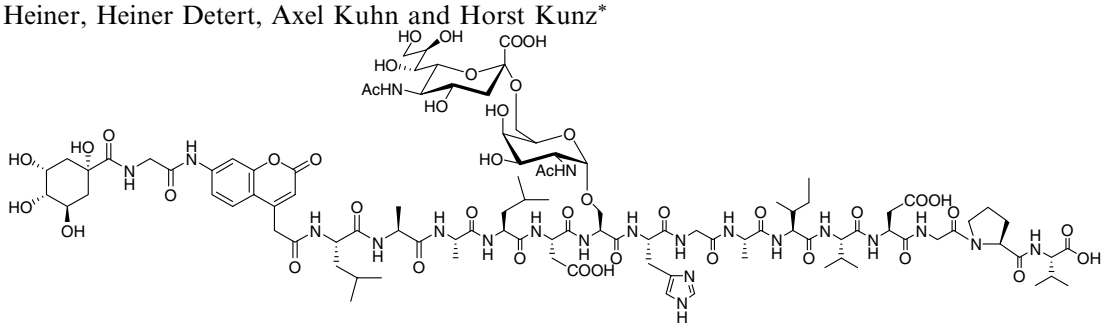
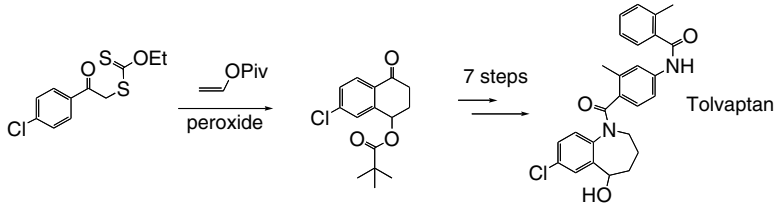
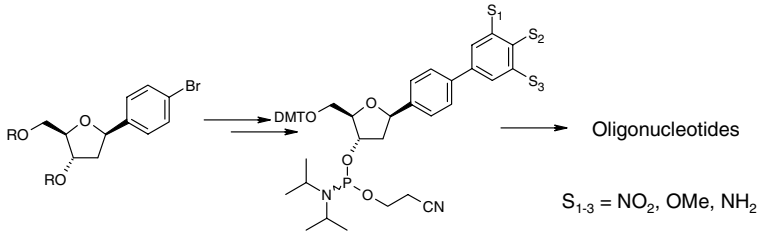
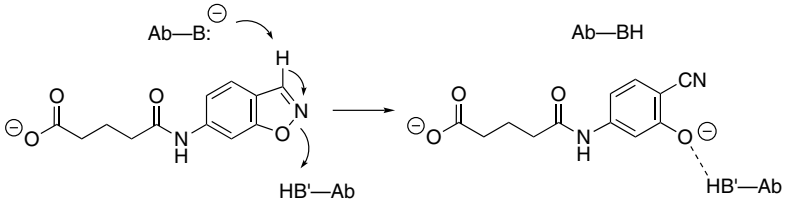
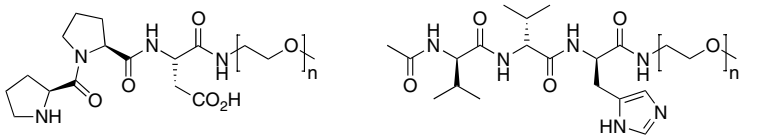


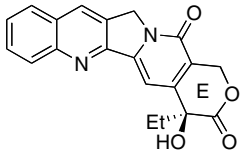


A flexible preparation of benzazepine derivatives using a series of radical and ionic reactions is reported. This approach was applied to the synthesis of tolvaptan, a very promising vasopressin V_2 receptor antagonist currently in clinical trials.

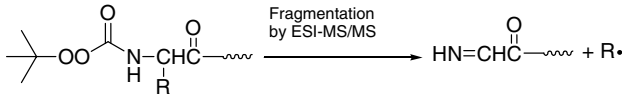


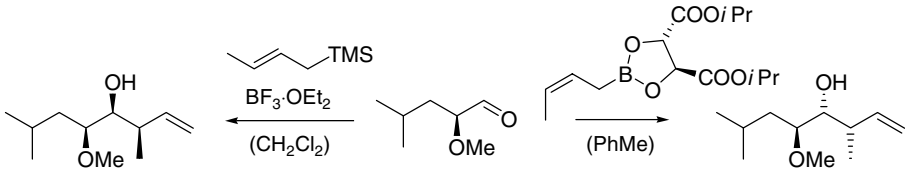


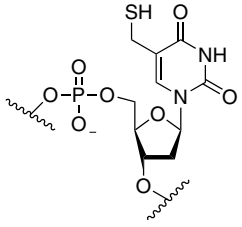


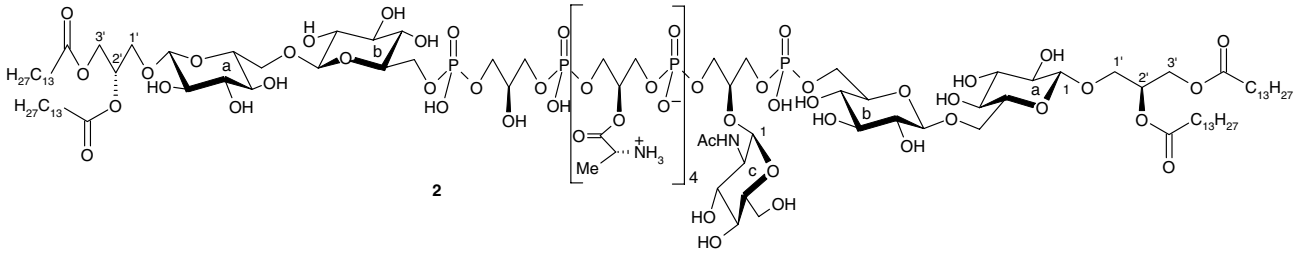


Analogs of the anti-tumor agent camptothecin with both closed E-rings (lactone and ether) and open E-rings (reduced acid, hydrazide, and protected Weinreb amide) have been prepared and tested in topoisomerase and cellular assays. The results provide insights into the structural features of the camptothecin E-ring that affect biological activity.









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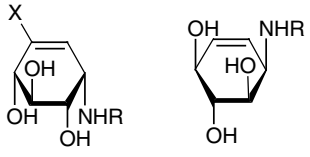
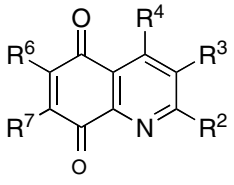


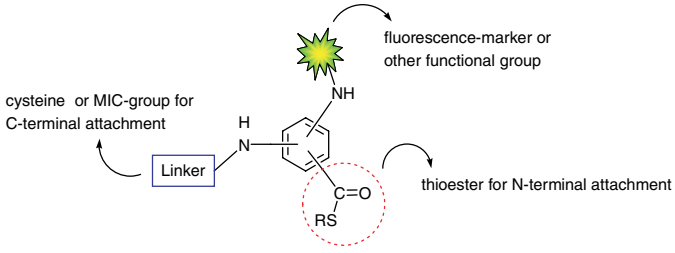
5: X = CH_2OH **(-)-10**

(+)-10: X = H

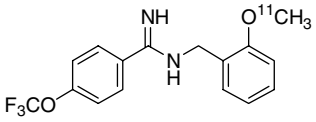
A solid-phase synthesis of new N-substituted valienamines has been developed and new synthesis of (−)-conduramine F-1, (+)-*ent*-conduramine F-1, and their N-derivatives is presented. The inhibitory activities of these new compounds toward α-glucosidases are compared.

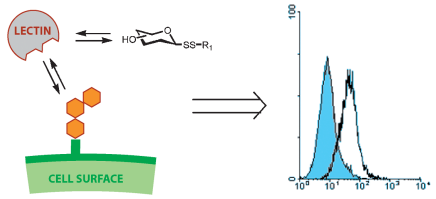


The structure–activity relationship of a focused series of C2-, C3-, or C4-modified quinoline-5,8-quinones on Cdc25B inhibition was interrogated in vitro. Two compounds also inhibited HeLa cell growth.



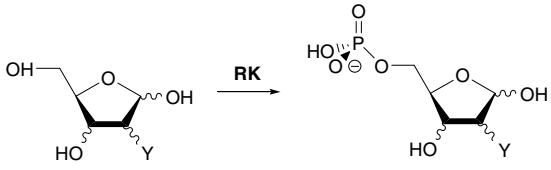
REGULAR ARTICLES

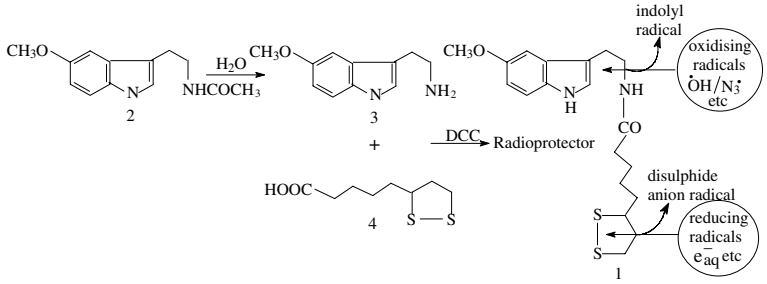


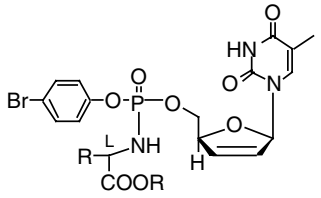


Binding of lectins to cell surface ligands triggers many medically relevant effects. Glycosyldisulfides from dynamic combinatorial libraries can interfere with these processes, as monitored by fluorescent cell assays.

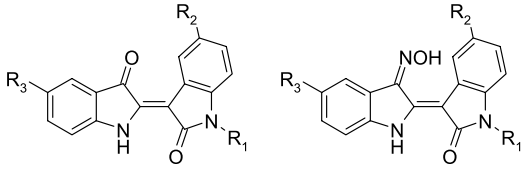
Ribokinase (RK) was expressed in the *Escherichia coli* ER2566 cells, purified from sonicated cells by double chromatography to afford a preparation with specific activity of 75μmol/minmg protein. Besides D-ribose and 2-deoxy-D-ribose, RK was found to catalyze the 5-*O*-phosphorylation of D-arabinose, D-xylose and D-fructose in the presence of ATP and potassium and magnesium ions; L-ribose and L-arabinose are not substrates for the recombinant enzyme. A new radiochemical method for monitoring the formation of D-ribofuranose-5-[^{32}P]phosphate in the presence of [γ-^{32}P]ATP and RK is reported.



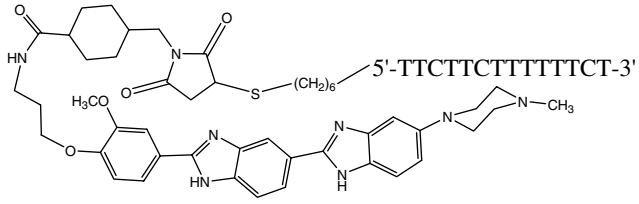




We examined the effect of cellular metabolism of three alkyl substituted amino acid ester phosphoramidate derivatives of stavudine in different cell lines. Marked cell-to-cell differences were found in both the rate of hydrolysis and chiral selectivity. This selectivity implies that different enzymes may be involved in the metabolism of these compounds depending on the cell type involved.



The effects of 34 new indirubin derivatives on CDK1/cyclin B, CDK5/p25, and GSK-3, as well as on SH-SY5Y human neuroblastoma cell survival, were investigated.



Conjugation of a bisbenzimidazole with DNA was done using SMCC, a heterobifunctional crosslinking reagent, by a simple methodology. Conjugate was characterized by ESMS. Triple helix formation studies were done with the conjugate.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Ribonucleotide Reductases (RNR) are radical-containing enzymes that catalyze the convertion of ribonucleotides to 2′-deoxyribonucleotides. The occurring intramolecular electron transfer is investigated by model peptides. The graphic was designed by Michael Graber from the Bernd Giese's research group using in part the following PDB entries: 1RLR (Uhlin, U., Eklund, H. *Nature* **1994**, *370*, 533–539) and 1XSM (Kauppi, B., Nielsen, B. B., Ramaswamy, S., Larsen, I. K., Thelander, M., Thelander, L., Eklund, H. *J. Mol. Biol.* **1996**, *262*, 706–720).

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