SUPPORTING INFORMATIONS

Semi-synthesis, biological activity and molecular modeling studies of C-ring modified camptothecins

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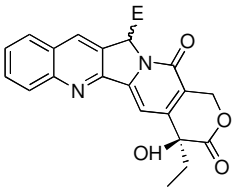
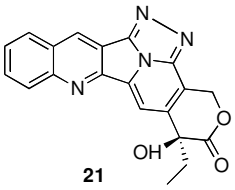
The synthesis, biological activity and molecular modeling studies of C-ring modified camptothecins are reported. A general synthetic protocol, based on the "C-5-CPT enolate chemistry", allowed to obtain diverse C5-substituted analogs. All new compounds, which were obtained as 1:1 epimeric mixtures, were tested for their antiproliferative activity. The collected data showed that all novel derivatives are less active than the references and that one of the two epimers is more active than the other. Molecular docking simulations were performed to achieve more insight into the interactions between the new C5-modified CPTs and Topo I. A good correlation was observed when the data of cytotoxicity and the values calculated for the free energy of binding were combined.



7,8,12, 15,16,18,22



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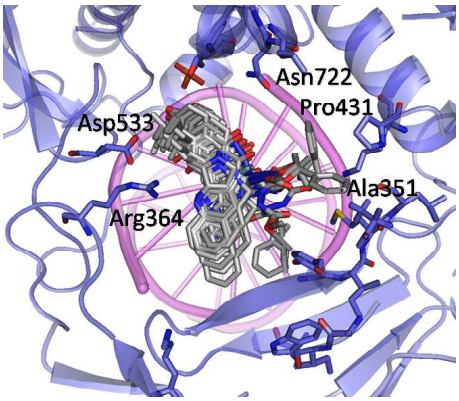

Contents

Elemental Analysis Data

Compound	Anal.	C calcd.	C found	H calcd.	H found	N calcd.	N found
4	$C_{26}H_{30}N_2O_4Si$	67,50	67,74	6,54	6,50	6,06	6,12
11a	$C_{26}H_{29}FN_2O_4Si$	64,98	64,80	6,08	6,13	5,83	5,79
11b	$C_{26}H_{29}FN_2O_4Si$	64,98	65,09	6,08	6,03	5,83	5,89
17a	$C_{26}H_{29}N_5O_4Si$	62,01	62,22	5,80	5,76	13,91	13,98
17b	$C_{26}H_{29}N_5O_4Si$	62,01	61,89	5,80	5,86	13,91	13,87
14a	$C_{36}H_{48}N_4O_8Si$	62,40	62,55	6,98	6,93	8,09	8,05
14b	$C_{36}H_{48}N_4O_8Si$	62,40	62,53	6,98	7,02	8,09	8,12
13a	$C_{42}H_{44}N_4O_8Si$	66,30	66,19	5,83	5,88	7,36	7,40
13b	$C_{42}H_{44}N_4O_8Si$	66,30	66,47	5,83	5,79	7,36	7,31
12a	$C_{20}H_{15}FN_2O_4$	65,57	65,30	4,13	4,09	7,65	7,61
12b	$C_{20}H_{15}FN_2O_4$	65,57	65,72	4,13	4,17	7,65	7,69
18a	$C_{20}H_{15}N_5O_4$	61,69	61.84	3,88	3,93	17,99	17,87
18b	$C_{20}H_{15}N_5O_4$	61,69	61.55	3,88	3,92	17,99	18,07
16a	$C_{30}H_{34}N_4O_8$	62,27	62,13	5,92	5,96	9,68	9,61
16b	$C_{30}H_{34}N_4O_8$	62,27	62,11	5,92	5,95	9,68	9,60
15a	$C_{36}H_{30}N_4O_8$	66,87	67,01	4,68	4,72	8,66	8,70
15b	$C_{36}H_{30}N_4O_8$	66,87	67,69	4,68	4,73	8,66	8,71
21	$C_{20}H_{14}N_4O_3$	67,03	67,19	3,94	3,99	15,63	15,71