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Chromophore-modified bis-benzo[g]indolecarboxamides: synthesis and citotoxicity of bis-benzo[g]indazole-3-carboxamides and related compounds.

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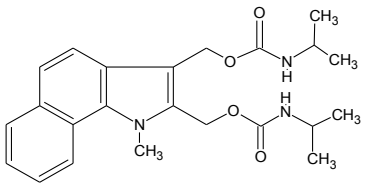
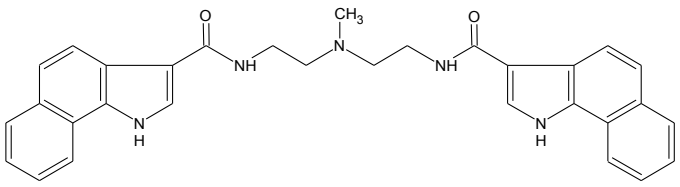
Cancer chemoteraphy continue to be an important research avenue. Combination chemotherapy using antineoplastic agents with different mechanisms of action is one method employed to combat this disease.

Thus, a single molecule containing two functional groups, each with a different mechanism of action, also could prove beneficial in cancer treatment.[1] In order to combine features of two of the most important drug classes in cancer therapy, intercalating and alkylating agents, the {2-({[(isopropylamino)carbonyl]

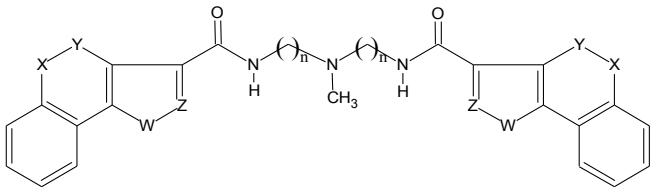
oxy}methyl)-1-methyl-1H-benzo[g]indol-3-yl-N-isopropylcarbamate (**1**) and the N_3-{2-[{2-[(1H-benzo[g]indol-3-yl-carbonyl)amino]ethyl}amino]ethyl}-1H-benzo[g]indole-3-carboxamide (**2**) were syn-thesized by us.[2a,b]



1, GI_{50}= 1.41 μ M



2, GI_{50}= 1.86 μ M



n : 2, 3

X-Y : CH=CH, CH_2

W-Z : HN-N, CH_3-N-, Ph-N-N

2,4-Cl_2Ar-N-N

3

These compounds possessed good growth inhibitory activity probably due to a double interaction with DNA: compound **1** contains both alkylating carbamic moieties and a mono intercalating benzo[g]indole portion while compound **2** contains two benzo[g]indole chromophores bridged by an aminobisalkylamide linker. In our continuing effort to search for novel bifunctional antitumor compounds, following the classical –CH=/–N= bioisosterism, we designed aza-analogues **3** of the bis-benzo[g]indole-3-carboxamide **2**.

Syntheses and biological results are reported.

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1. Goodman & Gilman's, *The pharmacological basis of therapeutics*, Ninth Edition, **1996**, 1233-1287

2a. Pinna, G.A.; Pirisi, M.A.; Sechi, M.; Paglietti, G. *Il Farmaco*, **1998**, *53*, 161-168.

b. Pinna, G.A. *et al*: unpublished results.