Spectroscopic studies of the interactions of 3,8-bis(3-aminoalkylamido)-5-ethyl-6-phenyl-5-phenanthridinium bromide derivatives with G-quadruplex DNA

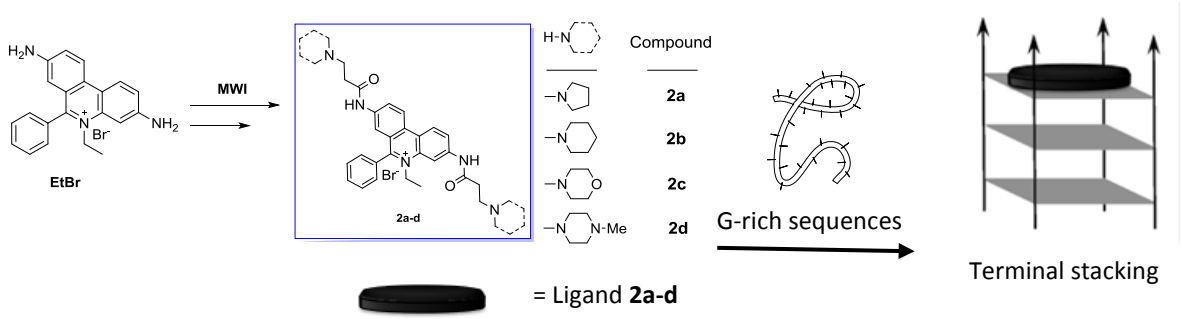
[1,2] Ergin Yalçın,[1] Halil Duyar,[2] Heiko Ihmels, [1] Zeynel Seferoğlu

[1] *Department of Chemistry, Faculty of Science, Gazi University, Teknikokullar, Ankara, Turkey.*

[2]*University of Siegen, Organic Chemistry II, Adolf-Reichwein-Str. 2, D-57068 Siegen, Germany*

Abstract: An improved microwave-induced synthesis of four 5-ethyl-6-phenyl-3,8-bis{[1-oxo-3-(alkylamino)propyl]amino}-5-phenanthridinium derivatives (Ethidium derivatives, 2a-d) is presented. As the derivatives **2a–d** have been proposed previously to be telomerase inhibitors, the binding interactions of these ethidium derivatives with G-quadruplex DNA were evaluated by means of photometric and fluorimetric titration, thermal DNA denaturation, CD and ^{1}H-NMR spectroscopy. In particular, the bis-pyrrolidin-1-ylpropanamido-substituted derivative **2a** exhibits high selectivity for quadruplex DNA relative to duplex DNA. Overall, the results show that ethidium derivatives such as **2a–d** are promising lead structures for the development of telomer-targeting drugs.

Introduction: The selective stabilization of G-quadruplex DNA (G4-DNA) by artificial ligands is a challenging task to identify biological important processes and also a useful strategy for the development of anti-cancer drugs because the formation of quadruplex structures may cause transcriptional repression of oncogenes and/or anti-telomerase activity in cancer cell. The ligands, derivatives of ethidium bromide, i.e. a classical DNA intercalator have been demonstrated to bind to quadruplex DNA with high affinity and to inhibit telomerase activity. The serious knowledge gap with regard to the telomerase inhibition by derivatives **2a**–**d** prompted us to perform the necessary complementary studies to get further insight into interactions of the bioactive ligands **2a**–**d** with quadruplex DNA[1]. In this study, an improved synthesis of the compounds **2a**–**d** along with spectroscopic studies of their binding interactions with quadruplex DNA.



Bibliography

[1] Yalcin E., *et all.*, Spectroscopic studies of the interactions of 3,8-bis (alkylamido) 5-ethyl -6-phenyl -5-phenanthridinium bromide derivatives with quadruplex DNA, Spectrochim. Acta, Part A. In press. https://doi.org/10.1016/j.saa.2018.02.051