Synthesis of (Z)-(arylamino)-pyrazolyl/isoxazolyl-2-propenones as Tubulin Targeting Anticancer Agents and Apoptotic Inducers

Ahmed Kamal, a Vangala Santhosh Reddy, a Anver Basha Shaik, a G. Bharath Kumar, a M V P S Vishnuvardhan, a Sowjanya Polepalli, b Nishant Jain b

a Medicinal Chemistry and Pharmacology, CSIR – Indian Institute of Chemical Technology, Hyderabad, Telangana- 500 007, India
b Centre for Chemical Biology CSIR-Indian Institute of Chemical Technology, Hyderabad, Telangana- 500 007, India

*Correspondence: ahmedkamal@iict.res.in; Phone: (+) 91-40-27193157; Fax: (+) 91-40-27193189.

Page No.
1H NMR Spectra........................................................................................................2-10
13C NMR Spectra.......................................................................................................11-20
HRMS Spectra............................................................................................................21-30
Effect of compounds 9a, 9b and Nocodazole (III) on caspase-3 activity........31

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry. This journal is © The Royal Society of Chemistry 2015
$^1$H NMR Spectra

Compound: 9a

Compound: 9b
Compound : 9c

Compound : 9d
Compound: 9g

Compound: 9h
Compound : 9i

Compound : 9j
Compound: 9k

Compound: 9l
Compound: **9o**

- Molecular structure of compound 9o with chemical shifts.

---

Compound: **9p**

- Molecular structure of compound 9p with chemical shifts.
Compound: 9q
$^{13}$C NMR Spectra
Compound: 9a

Compound: 9b
Compound: 9c

Compound: 9d
Compound: 9e

Compound: 9f
Compound : $9_g$

Compound : $9_h$
Compound: 9i

Compound: 9j
Compound: 9k

Compound: 9l
Compound : \(9o\)

Compound : \(9p\)
Compound: 9q
Compound: 9a

Compound: 9b
Compound: 9c

Compound: 9d
Compound: 9e

Compound: 9f
Compound : 9g

Compound : 9h
Compound: 9i

Compound: 9j
Compound: 9k

Compound: 9l
Compound : 9m

Compound : 9n
Compound: 9o

Compound: 9p
Compound: 9q
Caspase-3 activation

There are some reports that the cell cycle arrest at G2/M phase takes place by the induction of cellular apoptosis. Hence, it was considered of interest to understand the correlation of cytotoxicity with that to apoptosis by 9a and 9b. Cysteine aspartase group, namely, caspases play a crucial role in the induction of apoptosis and amongst them caspase-3 happens to be one of the effector caspase. Hence, we treated A-549 cells with 9a and 9b examined the activation of caspase-3. The results indicate that there is nearly 2-3.5 fold induction in caspase-3 activity in cells treated with these conjugates at 2 μM concentrations for 24 hrs. Therefore activation of caspase-3 by 9a and 9b indicate that they have the capacity to induce apoptosis in A-549.

Figure: Effect of compounds 9a and 9b on caspase-3 activity: A-549 cells were treated for 24 h with 2 μM concentrations of compounds 9a and 9b. Values indicated are the mean ± SD of two different experiments performed in triplicates.