SYNTHESIS AND CYTOTOXIC ACTIVITY OF SOME HETEROCYCLIC CHALCONES

Yordanka Ivanova\textsuperscript{a}, George Momekov\textsuperscript{b}, Ognyan Petrov\textsuperscript{a},
Margarita Karaivanova\textsuperscript{b}, Veneta Kalcheva\textsuperscript{a}

\textsuperscript{a}Faculty of Chemistry, Sofia University, 1164 Sofia, Bulgaria,
\textsuperscript{b}Faculty of Pharmacy, Medical University, Sofia 1000, Bulgaria

A variety of chalcones possess cytotoxicity towards a number of different tumor cell lines. While chalcone displayed minimal activity towards human colon adenocarcinoma cell line having an IC\textsubscript{50} figure greater than 100 \(\mu\)M, the related hydroxy compounds had IC\textsubscript{50} values in the range of 2-23 \(\mu\)M. In this study, we report the synthesis of new heterocyclic chalcones 3, including protected hydroxyl group in 1,3-oxazole cycle. Some Mannich bases reported recently, had more cytotoxicity than the corresponding chalcones. We prepared Mannich bases 4 of some of the heterocyclic chalcones 3.

\[
\begin{align*}
R^1 & \quad \text{N} \quad \text{O} \quad \text{O} \\
\text{1} & \quad \text{H}_2 \quad \text{C} \quad \text{N} \quad \text{O} \quad \text{O} \\
\text{2} & \quad \text{H}_2 \quad \text{C} \quad \text{N} \quad \text{O} \quad \text{O} \\
\text{3} & \quad \text{H}_2 \quad \text{C} \quad \text{N} \quad \text{O} \quad \text{O} \\
\text{4} & \quad \text{H}_2 \quad \text{C} \quad \text{N} \quad \text{O} \quad \text{O}
\end{align*}
\]

(a) CH\textsubscript{3}COCl, AlCl\textsubscript{3}-DMF; (b) aldehyde, aq. KOH, EtOH; (c) secondary amine, CH\textsubscript{2}O, EtOH

The compounds revealed a pronounced cytotoxic potential in BV-173 cells as assessed by the MTT assay. Preliminary data indicate that these chalcones trigger a necrotic type of programmed cell death as documented by DNA isolation, electrophoretic analysis, ethidium bromide staining and UV-transillumination. As a continuation of our systematic studies on 1,3-azoles, our present aim was the preparation and investigation of isomeres of the aforementioned compounds.

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\begin{align*}
R^1 & \quad \text{NHCCH}_3 \quad \text{O} \quad \text{O} \\
\text{OH} & \quad \text{H}_3 \quad \text{C} \quad \text{O} \quad \text{O} \\
\text{NHCOCH}_3 & \quad \text{H}_3 \quad \text{C} \quad \text{O} \quad \text{O} \\
\text{NHCH}_3 & \quad \text{H}_3 \quad \text{C} \quad \text{O} \quad \text{O} \\
\text{H}_3 \quad \text{C} & \quad \text{O} \quad \text{O} \\
\text{H}_3 \quad \text{C} & \quad \text{O} \quad \text{O} \\
\text{H}_3 \quad \text{C} & \quad \text{O} \quad \text{O} \\
\text{H}_3 \quad \text{C} & \quad \text{O} \quad \text{O} \\
\text{H}_3 \quad \text{C} & \quad \text{O} \quad \text{O}
\end{align*}
\]

(a) CH\textsubscript{3}COCl, AlCl\textsubscript{3}-DMF; (b) HCl; (c) 1,1’-Carbonyldiimidazole, THF; (d) aldehyde, aq. KOH, EtOH, r.t.