PHOSPHORUS, SULFUR, AND SILICON
AND THE RELATED ELEMENTS

EDITOR-IN-CHIEF:
ROBERT R. HOLMES
EUROPEAN EDITOR
L. MAIER

Proceedings of the Twenty-First
International Symposium on the
Organic Sulfur (ISOCS-XXI)

Guest Edited by Jose L. Garcia Ruano,
Juan Carlos Carretero, and
Ana M. Martin Castro
2-[(Carboxymethyl)sulfanyl]-4-oxo-4-arylbutoanoic Acids Suppressed Survival of Neoplastic Human HeLa Cells: A QSAR Study

Branko J. Drakulić
Institute for Chemistry, Technology and Metallurgy, Belgrade, Serbia and Montenegro

Zorica D. Juranić
Institute for Oncology and Radiology of Serbia, Belgrade, Serbia and Montenegro

Ivan O. Juranić
Faculty of Chemistry, University of Belgrade, Belgrade, Serbia and Montenegro

Fifteen 2-[(carboxymethyl)sulfanyl]-4-oxo-4-arylbutoanoic acids (Chart 1) were synthesized in Michael-type addition of the thioglycolic acid to series of \((E)\)-4-aryl-4-oxo-2-butoenoic acids.

\[
\text{CHART 1}
\]

The antiproliferative action of synthesized compounds against human cervix carcinoma, HeLa, cells was investigated. Target cells were continuously treated with increasing concentrations of substituted 2-[(carboxymethyl)-sulfanyl]-4-oxo-4-arylbutoanoic acids during three days. The MTT test\(^1\) was used for assessment of the antiproliferative action of the investigated compounds. The standard biological
response was defined as concentration of examined agents that induced a 50% decrease in cell survival (IC$_{50}$). 2-[[Carboxymethyl]-sulfanyl]-4-oxo-4-arylbutanoic acids affected the survival of HeLa cells in range of concentrations from 29.48 μM to 0.644 μM. The 2,3,4-tri-MeO-derivative exerted the lowest, whereas 2,5-di-i-Pr-derivative exerted the strongest activity.

IC$_{50}$ values have very good correlation with the lipophilicity of studied compounds, expressed as estimated log P values, exerting a strong structure–activity relationship of Hansch type with $r = 0.966$.

Estimation of logarithm of partition coefficient [n-Octanol/Water] log($P$) = log($K_{OW}$) was done by Crippen's fragmentation method.$^2$

Based on the conclusion that antiproliferative action of studied compounds toward HeLa cells was directly correlated with lipophilicity, synthesis of more lipophilic 2-[[carboxymethyl]sulfanyl]-4-oxo-4-arylbutanoic acids is in preparation. Our aim is the estimation of the optimal lipophilic value for antiproliferative action of title compounds against *human cervix carcinoma*, HeLa, cells *in vitro*.

REFERENCES

Phosphorus, Sulfur, and Silicon and the Related Elements