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### 2-[(Carboxymethyl)sulfanyl]-4-oxo-4-arylbutanoic Acids Suppressed Survival of Neoplastic Human HeLa Cells: A QSAR Study

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## 2-[(Carboxymethyl)sulfanyl]-4-oxo-4-arylbutanoic Acids Suppressed Survival of Neoplastic Human HeLa Cells: A QSAR Study

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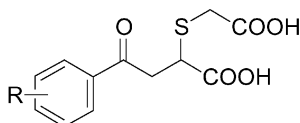
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Fifteen 2-[(carboxymethyl)sulfanyl]-4-oxo-4-arylbutanoic acids (Chart 1) were synthesized in Michael-type addition of the thioglycolic acid to series of (*E*)-4-aryl-4-oxo-2-butenic acids.



R = H-; 2,4-di-Me-; 3,4-di-Me-; 2,5-di-Me-; 4-Me-; 4-Et-; 4-*i*-Pr-; 2,5-di-*i*-Pr-; 4-*n*-Bu-; 4-*tert*-Bu-; 2-Cl-4-Me-; 4-F-; 4-Cl-; 4-Br-; 2,3,4-tri-MeO-

### 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-arylbutanoic acids during three days. The MTT test<sup>1</sup> was used for assessment of the antiproliferative action of the investigated compounds. The standard biological

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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  $\mu$ M to 0.644  $\mu$ M. 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.<sup>2</sup>

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*.

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