Synthesis and Anticancer Evaluation of Some Phenothiazine Derivatives[1]

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Abstract—10*H*-Phenothiazine **1** reacts with 2-chloroacetonitrile to give 2-(10*H*-phenothiazin-10-yl)-acetonitrile **2**, which upon reaction with sodium azide gives the corresponding tetrazole **3**. Treatment of **2** by either hydrazine hydrate or hydroxylamine affords 2-(2-chloro-10*H*-phenothiazin-10-yl)acetimidohydrazide **4** and 2-(2-chloro-10*H*-phenothiazin-10-yl)-*N*'-hydroxyacetimidamide **7**, respectively. Reaction of **4** with CS_2 leads to the thione derivative **5**. Treatment of **7** with acetic anhydride gives 3-[(2-chloro-10*H*-phenothiazin-10-yl)methyl]-4,5-dihydro-1,2,4-oxadiazole **8**. Alkylation of sodium salt of compounds **3**, **5**, **6**, or **8** by 1-chloro-2-methoxyethane and/or 2-(2-chloroethoxy)ethanol leads to the corresponding acyclic derivatives **9–16**. Structures of all newly synthesized compounds are confirmed by IR, NMR and mass spectroscopy. All of the synthesized compounds demonstrate high activity against breast cancer cell line (MCF7).

Keywords: phenothiazine, tetrazole, acyclic nucleosides, anticancer activity

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